

## Novel Compounds

5        This application is a continuation-in-part of Application No. 10/312,088 filed December 20, 2002, (now pending) which is the National Stage of International Application No. PCT/US01/19929, filed June 22, 2001, which claims the benefit of Provisional Application No. 60/213,161, filed June 22, 2000, and Provisional Application No. 60/213,156, filed June 22, 2000.

### Field of Invention

10        This invention relates to newly identified polypeptides and polynucleotides encoding such polypeptides, to their use in diagnosis and in identifying compounds that may be agonists, antagonists that are potentially useful in therapy, and to production of such polypeptides and polynucleotides. The polynucleotides and polypeptides of the present invention also relate to proteins with signal sequences which allow them to be secreted extracellularly or membrane-associated (hereinafter often referred collectively as secreted proteins or secreted polypeptides).

### Background of the Invention

20        The drug discovery process is currently undergoing a fundamental revolution as it embraces "functional genomics", that is, high throughput genome- or gene-based biology. This approach as a means to identify genes and gene products as therapeutic targets is rapidly superseding earlier approaches based on "positional cloning". A phenotype, that is a biological function or genetic disease, would be identified and this would then be tracked back to the responsible gene, based on its genetic map position.

25        Functional genomics relies heavily on high-throughput DNA sequencing technologies and the various tools of bioinformatics to identify gene sequences of potential interest from the many molecular biology databases now available. There is a continuing need to identify and characterise further genes and their related polypeptides/proteins, as targets for drug discovery.

30        Proteins and polypeptides that are naturally secreted into blood, lymph and other body fluids, or secreted into the cellular membrane are of primary interest for research and development of protein therapeutic agents. The reason for this interest is the relative ease to target secreted protein therapeutics into their place of action (body fluids or the cellular membrane). Secreted proteins, and the extracellular regions of transmembrane proteins, can be directly administered into body fluids, or can be directed to body fluids or membranes by a natural pathway. The natural pathway for protein secretion into extracellular space is the endoplasmic reticulum in eukaryotes and the inner membrane in prokaryotes (Palade, 1975, Science, 189, 347; Milstein, Brownlee, Harrison, and Mathews, 1972, Nature New Biol., 239, 117; Blobel, and Dobberstein, 1975, J. Cell. Biol., 67, 835). On the other hand, there is no known natural pathway for exporting a protein from

the exterior of the cells into the cytosol (with the exception of pinocytosis, a mechanism of snake venom toxin intrusion into cells). Therefore targeting protein therapeutics into cells poses extreme difficulties.

The secreted and membrane-associated proteins include but are not limited to all peptide hormones and their receptors (including but not limited to insulin, growth hormones, chemokines, cytokines, colony-stimulating factors such as erythropoietin, neuropeptides, integrins, kallikreins, lamins, melanins, natriuretic hormones, neuropsin, neurotrophins, pituitary hormones, pleiotrophins, prostaglandins, secretogranins, selectins, thromboglobulins, thymosins), cytokine receptors, the breast and colon cancer gene products, the obesity gene protein leptin and its receptors, serum albumin, superoxide dismutase, spliceosome proteins, 7TM (transmembrane) proteins also called as G-protein coupled receptors, immunoglobulins, several families of serine proteinases (including but not limited to proteins of the blood coagulation cascade, digestive enzymes), deoxyribonuclease I, etc.

Therapeutics based on secreted or membrane-associated proteins approved by FDA or foreign agencies include but are not limited to insulin, glucagon, growth hormone, chorionic gonadotropin, follicle stimulating hormone, luteinizing hormone, calcitonin, adrenocorticotrophic hormone (ACTH), vasopressin, interleukines, interferons, erythropoietin, the extracellular region of the transmembrane cytokine receptor TNFalpha (soluble TNFalpha receptor or Enbrel), immunoglobulins, lactoferrin (diverse products marketed by several companies), tissue-type plasminogen activator (Alteplase by Genentech), hyaluronidase (Wydase by Wyeth-Ayerst), dornase alpha (Pulmozyme by Genentech), Chymodiactin (chymopapain by Knoll), alglucerase (Ceredase by Genzyme), streptokinase (Kabikinase by Pharmacia) (Streptase by Astra), etc. This indicates that secreted and membrane-associated proteins have an established, proven history as therapeutic targets. Clearly, there is a need for identification and characterization of further secreted and membrane-associated proteins which can play a role in preventing, ameliorating or correcting dysfunction or disease, including but not limited to diabetes, breast-, prostate-, colon cancer and other malignant tumors, hyper- and hypotension, obesity, bulimia, anorexia, growth abnormalities, asthma, manic depression, dementia, delirium, mental retardation, Huntington's disease, Tourette's syndrome, schizophrenia, growth, mental or sexual development disorders, and dysfunctions of the blood cascade system including those leading to stroke. The proteins of the present invention which include the signal sequences are also useful to further elucidate the mechanism of protein transport which at present is not entirely understood, and thus can be used as research tools.

### Summary of the Invention

The present invention relates to particular polypeptides and polynucleotides of the genes set forth in Table I, including recombinant materials and methods for their production. Such polypeptides and polynucleotides are of interest in relation to methods of treatment of certain diseases, including, but not limited to, the diseases set forth in Tables III and V, hereinafter referred to as "diseases of the invention". In a further aspect, the invention relates to methods for identifying agonists and antagonists (*e.g.*, inhibitors) using the materials provided by the invention, and treating conditions associated with imbalance of polypeptides and/or polynucleotides of the genes set forth in Table I with the identified compounds. In still a further aspect, the invention relates to diagnostic assays for detecting diseases associated with inappropriate activity or levels of the genes set forth in Table I. Another aspect of the invention concerns a polynucleotide comprising any of the nucleotide sequences set forth in the Sequence Listing and a polypeptide comprising a polypeptide encoded by the nucleotide sequence. In another aspect, the invention relates to a polypeptide comprising any of the polypeptide sequences set forth in the Sequence Listing and recombinant materials and methods for their production. Another aspect of the invention relates to methods for using such polypeptides and polynucleotides. Such uses include the treatment of diseases, abnormalities and disorders (hereinafter simply referred to as diseases) caused by abnormal expression, production, function and or metabolism of the genes of this invention, and such diseases are readily apparent by those skilled in the art from the homology to other proteins disclosed for each attached sequence. In still another aspect, the invention relates to methods to identify agonists and antagonists using the materials provided by the invention, and treating conditions associated with the imbalance with the identified compounds. Yet another aspect of the invention relates to diagnostic assays for detecting diseases associated with inappropriate activity or levels of the secreted proteins of the present invention.

### Brief Description of the Figure

Figure 1 demonstrates enhancement of would closure in ob/ob mice by administration of an adenovirus encoding in its genome  $\beta$ -Tectorin.

### Description of the Invention

In a first aspect, the present invention relates to polypeptides the genes set forth in Table I. Such polypeptides include:

- (a) an isolated polypeptide encoded by a polynucleotide comprising a sequence set forth in the Sequence Listing;

- (b) an isolated polypeptide comprising a polypeptide sequence having at least 95%, 96%, 97%, 98%, or 99% identity to a polypeptide sequence set forth in the Sequence Listing;
- (c) an isolated polypeptide comprising a polypeptide sequence set forth in the Sequence Listing;
- (d) an isolated polypeptide having at least 95%, 96%, 97%, 98%, or 99% identity to a polypeptide sequence set forth in the Sequence Listing;
- (e) a polypeptide sequence set forth in the Sequence Listing; and
- (f) an isolated polypeptide having or comprising a polypeptide sequence that has an Identity Index of 0.95, 0.96, 0.97, 0.98, or 0.99 compared to a polypeptide sequence set forth in the Sequence Listing;

- (g) fragments and variants of such polypeptides in (a) to (f).

Polypeptides of the present invention are believed to be members of the gene families set forth in Table II. They are therefore of therapeutic and diagnostic interest for the reasons set forth in Tables III and V. The biological properties of the polypeptides and polynucleotides of the genes set forth in Table I are hereinafter referred to as "the biological activity" of polypeptides and polynucleotides of the genes set forth in Table I. Preferably, a polypeptide of the present invention exhibits at least one biological activity of the genes set forth in Table I.

Polypeptides of the present invention also include variants of the aforementioned polypeptides, including all allelic forms and splice variants. Such polypeptides vary from the reference polypeptide by insertions, deletions, and substitutions that may be conservative or non-conservative, or any combination thereof. Particularly preferred variants are those in which several, for instance from 50 to 30, from 30 to 20, from 20 to 10, from 10 to 5, from 5 to 3, from 3 to 2, from 2 to 1 or 1 amino acids are inserted, substituted, or deleted, in any combination.

Preferred fragments of polypeptides of the present invention include an isolated polypeptide comprising an amino acid sequence having at least 30, 50 or 100 contiguous amino acids from an amino acid sequence set forth in the Sequence Listing, or an isolated polypeptide comprising an amino acid sequence having at least 30, 50 or 100 contiguous amino acids truncated or deleted from an amino acid sequence set forth in the Sequence Listing. Preferred fragments are biologically active fragments that mediate the biological activity of polypeptides and polynucleotides of the genes set forth in Table I, including those with a similar activity or an improved activity, or with a decreased undesirable activity. Also preferred are those fragments that are antigenic or immunogenic in an animal, especially in a human.

Fragments of a polypeptide of the invention may be employed for producing the corresponding full-length polypeptide by peptide synthesis; therefore, these variants may be employed as intermediates for producing the full-length polypeptides of the invention. A polypeptide of the present invention may be in the form of the "mature" protein or may be a part of

a larger protein such as a precursor or a fusion protein. It is often advantageous to include an additional amino acid sequence that contains secretory or leader sequences, pro-sequences, sequences that aid in purification, for instance multiple histidine residues, or an additional sequence for stability during recombinant production.

5 Polypeptides of the present invention can be prepared in any suitable manner, for instance by isolation from naturally occurring sources, from genetically engineered host cells comprising expression systems (*vide infra*) or by chemical synthesis, using for instance automated peptide synthesizers, or a combination of such methods. Means for preparing such polypeptides are well understood in the art.

10 In a further aspect, the present invention relates to polynucleotides of the genes set forth in Table I. Such polynucleotides include:

- (a) an isolated polynucleotide comprising a polynucleotide sequence having at least 95%, 96%, 97%, 98%, or 99% identity to a polynucleotide sequence set forth in the Sequence Listing;
  - (b) an isolated polynucleotide comprising a polynucleotide set forth in the Sequence Listing;
  - 15 (c) an isolated polynucleotide having at least 95%, 96%, 97%, 98%, or 99% identity to a polynucleotide set forth in the Sequence Listing;
  - (d) an isolated polynucleotide set forth in the Sequence Listing;
  - (e) an isolated polynucleotide comprising a polynucleotide sequence encoding a polypeptide sequence having at least 95%, 96%, 97%, 98%, or 99% identity to a polypeptide sequence set forth
  - 20 in the Sequence Listing;
  - (f) an isolated polynucleotide comprising a polynucleotide sequence encoding a polypeptide set forth in the Sequence Listing;
  - (g) an isolated polynucleotide having a polynucleotide sequence encoding a polypeptide sequence having at least 95%, 96%, 97%, 98%, or 99% identity to a polypeptide sequence set forth in the
  - 25 Sequence Listing;
  - (h) an isolated polynucleotide encoding a polypeptide set forth in the Sequence Listing;
  - (i) an isolated polynucleotide having or comprising a polynucleotide sequence that has an Identity Index of 0.95, 0.96, 0.97, 0.98, or 0.99 compared to a polynucleotide sequence set forth in the Sequence Listing;
  - 30 (j) an isolated polynucleotide having or comprising a polynucleotide sequence encoding a polypeptide sequence that has an Identity Index of 0.95, 0.96, 0.97, 0.98, or 0.99 compared to a polypeptide sequence set forth in the Sequence Listing; and
- polynucleotides that are fragments and variants of the above mentioned polynucleotides or that are complementary to above mentioned polynucleotides, over the entire length thereof.

Preferred fragments of polynucleotides of the present invention include an isolated polynucleotide comprising an nucleotide sequence having at least 15, 30, 50 or 100 contiguous nucleotides from a sequence set forth in the Sequence Listing, or an isolated polynucleotide comprising a sequence having at least 30, 50 or 100 contiguous nucleotides truncated or deleted from a sequence set forth in the Sequence Listing.

Preferred variants of polynucleotides of the present invention include splice variants, allelic variants, and polymorphisms, including polynucleotides having one or more single nucleotide polymorphisms (SNPs).

Polynucleotides of the present invention also include polynucleotides encoding polypeptide variants that comprise an amino acid sequence set forth in the Sequence Listing and in which several, for instance from 50 to 30, from 30 to 20, from 20 to 10, from 10 to 5, from 5 to 3, from 3 to 2, from 2 to 1 or 1 amino acid residues are substituted, deleted or added, in any combination. In a further aspect, the present invention provides polynucleotides that are RNA transcripts of the DNA sequences of the present invention. Accordingly, there is provided an RNA polynucleotide that:

(a) comprises an RNA transcript of the DNA sequence encoding a polypeptide set forth in the Sequence Listing;

(b) is a RNA transcript of a DNA sequence encoding a polypeptide set forth in the Sequence Listing;

(c) comprises an RNA transcript of a DNA sequence set forth in the Sequence Listing; or

(d) is a RNA transcript of a DNA sequence set forth in the Sequence Listing;

and RNA polynucleotides that are complementary thereto.

The polynucleotide sequences set forth in the Sequence Listing show homology with the polynucleotide sequences set forth in Table II. A polynucleotide sequence set forth in the Sequence Listing is a cDNA sequence that encodes a polypeptide set forth in the Sequence Listing. A polynucleotide sequence encoding a polypeptide set forth in the Sequence Listing may be identical to a polypeptide encoding a sequence set forth in the Sequence Listing or it may be a sequence other than a sequence set forth in the Sequence Listing, which, as a result of the redundancy (degeneracy) of the genetic code, also encodes a polypeptide set forth in the Sequence Listing. A polypeptide of a sequence set forth in the Sequence Listing is related to other proteins of the gene families set forth in Table II, having homology and/or structural similarity with the polypeptides set forth in Table II. Preferred polypeptides and polynucleotides of the present invention are expected to have, *inter alia*, similar biological functions/properties to their homologous polypeptides and polynucleotides. Furthermore, preferred polypeptides and polynucleotides of the present invention have at least one activity of the genes set forth in Table I.

Polynucleotides of the present invention may be obtained using standard cloning and screening techniques from a cDNA library derived from mRNA from the tissues set forth in Table IV (see for instance, Sambrook *et al.*, Molecular Cloning: A Laboratory Manual, 2nd Ed., Cold Spring Harbor Laboratory Press, Cold Spring Harbor, N.Y. (1989)). Polynucleotides of the invention can also be obtained from natural sources such as genomic DNA libraries or can be synthesized using well known and commercially available techniques.

When polynucleotides of the present invention are used for the recombinant production of polypeptides of the present invention, the polynucleotide may include the coding sequence for the mature polypeptide, by itself, or the coding sequence for the mature polypeptide in reading frame with other coding sequences, such as those encoding a leader or secretory sequence, a pre-, or pro- or prepro- protein sequence, or other fusion peptide portions. For example, a marker sequence that facilitates purification of the fused polypeptide can be encoded. In certain preferred embodiments of this aspect of the invention, the marker sequence is a hexa-histidine peptide, as provided in the pQE vector (Qiagen, Inc.) and described in Gentz *et al.*, Proc Natl Acad Sci USA (1989) 86:821-824, or is an HA tag. A polynucleotide may also contain non-coding 5' and 3' sequences, such as transcribed, non-translated sequences, splicing and polyadenylation signals, ribosome binding sites and sequences that stabilize mRNA.

Polynucleotides that are identical, or have sufficient identity to a polynucleotide sequence set forth in the Sequence Listing, may be used as hybridization probes for cDNA and genomic DNA or as primers for a nucleic acid amplification reaction (for instance, PCR). Such probes and primers may be used to isolate full-length cDNAs and genomic clones encoding polypeptides of the present invention and to isolate cDNA and genomic clones of other genes (including genes encoding paralogs from human sources and orthologs and paralogs from other species) that have a high sequence similarity to sequences set forth in the Sequence Listing, typically at least 95% identity. Preferred probes and primers will generally comprise at least 15 nucleotides, preferably, at least 30 nucleotides and may have at least 50, if not at least 100 nucleotides. Particularly preferred probes will have between 30 and 50 nucleotides. Particularly preferred primers will have between 20 and 25 nucleotides.

A polynucleotide encoding a polypeptide of the present invention, including homologs from other species, may be obtained by a process comprising the steps of screening a library under stringent hybridization conditions with a labeled probe having a sequence set forth in the Sequence Listing or a fragment thereof, preferably of at least 15 nucleotides; and isolating full-length cDNA and genomic clones containing the polynucleotide sequence set forth in the Sequence Listing. Such hybridization techniques are well known to the skilled artisan. Preferred stringent hybridization conditions include overnight incubation at 42°C in a solution comprising: 50% formamide, 5xSSC

(150mM NaCl, 15mM trisodium citrate), 50 mM sodium phosphate (pH 7.6), 5x Denhardt's solution, 10 % dextran sulfate, and 20 microgram/ml denatured, sheared salmon sperm DNA; followed by washing the filters in 0.1x SSC at about 65°C. Thus the present invention also includes isolated polynucleotides, preferably with a nucleotide sequence of at least 100, obtained  
5 by screening a library under stringent hybridization conditions with a labeled probe having the sequence set forth in the Sequence Listing or a fragment thereof, preferably of at least 15 nucleotides.

The skilled artisan will appreciate that, in many cases, an isolated cDNA sequence will be incomplete, in that the region coding for the polypeptide does not extend all the way through to the  
10 5' terminus. This is a consequence of reverse transcriptase, an enzyme with inherently low "processivity" (a measure of the ability of the enzyme to remain attached to the template during the polymerisation reaction), failing to complete a DNA copy of the mRNA template during first strand cDNA synthesis.

There are several methods available and well known to those skilled in the art to obtain  
15 full-length cDNAs, or extend short cDNAs, for example those based on the method of Rapid Amplification of cDNA ends (RACE) (see, for example, Frohman et al., Proc Nat Acad Sci USA 85, 8998-9002, 1988). Recent modifications of the technique, exemplified by the Marathon (trade mark) technology (Clontech Laboratories Inc.) for example, have significantly simplified the search for longer cDNAs. In the Marathon (trade mark) technology, cDNAs have been prepared from  
20 mRNA extracted from a chosen tissue and an 'adaptor' sequence ligated onto each end. Nucleic acid amplification (PCR) is then carried out to amplify the "missing" 5' end of the cDNA using a combination of gene specific and adaptor specific oligonucleotide primers. The PCR reaction is then repeated using 'nested' primers, that is, primers designed to anneal within the amplified product (typically an adapter specific primer that anneals further 3' in the adaptor sequence and a  
25 gene specific primer that anneals further 5' in the known gene sequence). The products of this reaction can then be analyzed by DNA sequencing and a full-length cDNA constructed either by joining the product directly to the existing cDNA to give a complete sequence, or carrying out a separate full-length PCR using the new sequence information for the design of the 5' primer.

Recombinant polypeptides of the present invention may be prepared by processes well  
30 known in the art from genetically engineered host cells comprising expression systems. Accordingly, in a further aspect, the present invention relates to expression systems comprising a polynucleotide or polynucleotides of the present invention, to host cells which are genetically engineered with such expression systems and to the production of polypeptides of the invention by recombinant techniques. Cell-free translation systems can also be employed to produce such  
35 proteins using RNAs derived from the DNA constructs of the present invention.



For recombinant production, host cells can be genetically engineered to incorporate expression systems or portions thereof for polynucleotides of the present invention. Polynucleotides may be introduced into host cells by methods described in many standard laboratory manuals, such as Davis et al., Basic Methods in Molecular Biology (1986) and Sambrook *et al.*(*ibid*). Preferred methods of introducing polynucleotides into host cells include, for instance, calcium phosphate transfection, DEAE-dextran mediated transfection, transvection, micro-injection, cationic lipid-mediated transfection, electroporation, transduction, scrape loading, ballistic introduction or infection.

Representative examples of appropriate hosts include bacterial cells, such as *Streptococci*, *Staphylococci*, *E. coli*, *Streptomyces* and *Bacillus subtilis* cells; fungal cells, such as yeast cells and *Aspergillus* cells; insect cells such as *Drosophila* S2 and *Spodoptera* Sf9 cells; animal cells such as CHO, COS, HeLa, C127, 3T3, BHK, HEK 293 and Bowes melanoma cells; and plant cells.

A great variety of expression systems can be used, for instance, chromosomal, episomal and virus-derived systems, *e.g.*, vectors derived from bacterial plasmids, from bacteriophage, from transposons, from yeast episomes, from insertion elements, from yeast chromosomal elements, from viruses such as baculoviruses, papova viruses, such as SV40, vaccinia viruses, adenoviruses, adeno-associated viruses, fowl pox viruses, pseudorabies viruses and retroviruses, and vectors derived from combinations thereof, such as those derived from plasmid and bacteriophage genetic elements, such as cosmids and phagemids. The expression systems may contain control regions that regulate as well as engender expression. Generally, any system or vector that is able to maintain, propagate or express a polynucleotide to produce a polypeptide in a host may be used. The appropriate polynucleotide sequence may be inserted into an expression system by any of a variety of well-known and routine techniques, such as, for example, those set forth in Sambrook *et al.*, (*ibid*). Appropriate secretion signals may be incorporated into the desired polypeptide to allow secretion of the translated protein into the lumen of the endoplasmic reticulum, the periplasmic space or the extracellular environment. These signals may be endogenous to the polypeptide or they may be heterologous signals.

If a polypeptide of the present invention is to be expressed for use in screening assays, it is generally preferred that the polypeptide be produced at the surface of the cell. In this event, the cells may be harvested prior to use in the screening assay. If the polypeptide is secreted into the medium, the medium can be recovered in order to recover and purify the polypeptide. If produced intracellularly, the cells must first be lysed before the polypeptide is recovered.

Polypeptides of the present invention can be recovered and purified from recombinant cell cultures by well-known methods including ammonium sulfate or ethanol precipitation, acid extraction, anion or cation exchange chromatography, phosphocellulose chromatography,

hydrophobic interaction chromatography, affinity chromatography, hydroxylapatite chromatography and lectin chromatography. Most preferably, high performance liquid chromatography is employed for purification. Well known techniques for refolding proteins may be employed to regenerate active conformation when the polypeptide is denatured during intracellular synthesis, isolation and/or purification.

Polynucleotides of the present invention may be used as diagnostic reagents, through detecting mutations in the associated gene. Detection of a mutated form of a gene is characterized by the polynucleotides set forth in the Sequence Listing in the cDNA or genomic sequence and which is associated with a dysfunction. Will provide a diagnostic tool that can add to, or define, a diagnosis of a disease, or susceptibility to a disease, which results from under-expression, over-expression or altered spatial or temporal expression of the gene. Individuals carrying mutations in the gene may be detected at the DNA level by a variety of techniques well known in the art.

Nucleic acids for diagnosis may be obtained from a subject's cells, such as from blood, urine, saliva, tissue biopsy or autopsy material. The genomic DNA may be used directly for detection or it may be amplified enzymatically by using PCR, preferably RT-PCR, or other amplification techniques prior to analysis. RNA or cDNA may also be used in similar fashion. Deletions and insertions can be detected by a change in size of the amplified product in comparison to the normal genotype. Point mutations can be identified by hybridizing amplified DNA to labeled nucleotide sequences of the genes set forth in Table I. Perfectly matched sequences can be distinguished from mismatched duplexes by RNase digestion or by differences in melting temperatures. DNA sequence difference may also be detected by alterations in the electrophoretic mobility of DNA fragments in gels, with or without denaturing agents, or by direct DNA sequencing (see, for instance, Myers *et al.*, Science (1985) 230:1242). Sequence changes at specific locations may also be revealed by nuclease protection assays, such as RNase and S1 protection or the chemical cleavage method (see Cotton *et al.*, Proc Natl Acad Sci USA (1985) 85: 4397-4401).

An array of oligonucleotides probes comprising polynucleotide sequences or fragments thereof of the genes set forth in Table I can be constructed to conduct efficient screening of *e.g.*, genetic mutations. Such arrays are preferably high density arrays or grids. Array technology methods are well known and have general applicability and can be used to address a variety of questions in molecular genetics including gene expression, genetic linkage, and genetic variability, see, for example, M. Chee *et al.*, Science, 274, 610-613 (1996) and other references cited therein. Detection of abnormally decreased or increased levels of polypeptide or mRNA expression may also be used for diagnosing or determining susceptibility of a subject to a disease of the invention. Decreased or increased expression can be measured at the RNA level using any of the methods well

known in the art for the quantitation of polynucleotides, such as, for example, nucleic acid amplification, for instance PCR, RT-PCR, RNase protection, Northern blotting and other hybridization methods. Assay techniques that can be used to determine levels of a protein, such as a polypeptide of the present invention, in a sample derived from a host are well-known to those of skill in the art. Such assay methods include radio-immunoassays, competitive-binding assays, Western Blot analysis and ELISA assays.

Thus in another aspect, the present invention relates to a diagnostic kit comprising:

- (a) a polynucleotide of the present invention, preferably the nucleotide sequence set forth in the Sequence Listing, or a fragment or an RNA transcript thereof;
- (b) a nucleotide sequence complementary to that of (a);
- (c) a polypeptide of the present invention, preferably the polypeptide set forth in the Sequence Listing or a fragment thereof; or
- (d) an antibody to a polypeptide of the present invention, preferably to the polypeptide set forth in the Sequence Listing.

It will be appreciated that in any such kit, (a), (b), (c) or (d) may comprise a substantial component. Such a kit will be of use in diagnosing a disease or susceptibility to a disease, particularly diseases of the invention, amongst others.

The polynucleotide sequences of the present invention are valuable for chromosome localisation studies. The sequences set forth in the Sequence Listing are specifically targeted to, and can hybridize with, a particular location on an individual human chromosome. The mapping of relevant sequences to chromosomes according to the present invention is an important first step in correlating those sequences with gene associated disease. Once a sequence has been mapped to a precise chromosomal location, the physical position of the sequence on the chromosome can be correlated with genetic map data. Such data are found in, for example, V. McKusick, Mendelian Inheritance in Man (available on-line through Johns Hopkins University Welch Medical Library). The relationship between genes and diseases that have been mapped to the same chromosomal region are then identified through linkage analysis (co-inheritance of physically adjacent genes). Precise human chromosomal localisations for a genomic sequence (gene fragment etc.) can be determined using Radiation Hybrid (RH) Mapping (Walter, M. Spillett, D., Thomas, P., Weissenbach, J., and Goodfellow, P., (1994) A method for constructing radiation hybrid maps of whole genomes, *Nature Genetics* 7, 22-28). A number of RH panels are available from Research Genetics (Huntsville, AL, USA) e.g. the GeneBridge4 RH panel (*Hum Mol Genet* 1996 Mar;5(3):339-46 A radiation hybrid map of the human genome. Gyapay G, Schmitt K, Fizames C, Jones H, Vega-Czarny N, Spillett D, Muselet D, Prud'Homme JF, Dib C, Auffray C, Morissette J, Weissenbach J, Goodfellow PN). To determine the chromosomal location of a gene using this

panel, 93 PCRs are performed using primers designed from the gene of interest on RH DNAs. Each of these DNAs contains random human genomic fragments maintained in a hamster background (human / hamster hybrid cell lines). These PCRs result in 93 scores indicating the presence or absence of the PCR product of the gene of interest. These scores are compared with scores created using PCR products from genomic sequences of known location. This comparison is conducted at <http://www.genome.wi.mit.edu/>.

The polynucleotide sequences of the present invention are also valuable tools for tissue expression studies. Such studies allow the determination of expression patterns of polynucleotides of the present invention which may give an indication as to the expression patterns of the encoded polypeptides in tissues, by detecting the mRNAs that encode them. The techniques used are well known in the art and include in situ hybridization techniques to clones arrayed on a grid, such as cDNA microarray hybridization (Schena *et al*, Science, 270, 467-470, 1995 and Shalon *et al*, Genome Res, 6, 639-645, 1996) and nucleotide amplification techniques such as PCR. A preferred method uses the TAQMAN (Trade mark) technology available from Perkin Elmer. Results from these studies can provide an indication of the normal function of the polypeptide in the organism. In addition, comparative studies of the normal expression pattern of mRNAs with that of mRNAs encoded by an alternative form of the same gene (for example, one having an alteration in polypeptide coding potential or a regulatory mutation) can provide valuable insights into the role of the polypeptides of the present invention, or that of inappropriate expression thereof in disease. Such inappropriate expression may be of a temporal, spatial or simply quantitative nature.

A further aspect of the present invention relates to antibodies. The polypeptides of the invention or their fragments, or cells expressing them, can be used as immunogens to produce antibodies that are immunospecific for polypeptides of the present invention. The term "immunospecific" means that the antibodies have substantially greater affinity for the polypeptides of the invention than their affinity for other related polypeptides in the prior art.

Antibodies generated against polypeptides of the present invention may be obtained by administering the polypeptides or epitope-bearing fragments, or cells to an animal, preferably a non-human animal, using routine protocols. For preparation of monoclonal antibodies, any technique which provides antibodies produced by continuous cell line cultures can be used. Examples include the hybridoma technique (Kohler, G. and Milstein, C., Nature (1975) 256:495-497), the trioma technique, the human B-cell hybridoma technique (Kozbor *et al*, Immunology Today (1983) 4:72) and the EBV-hybridoma technique (Cole *et al*, Monoclonal Antibodies and Cancer Therapy, 77-96, Alan R. Liss, Inc., 1985).

Techniques for the production of single chain antibodies, such as those described in U.S. Patent No. 4,946,778, can also be adapted to produce single chain antibodies to polypeptides of this

invention. Also, transgenic mice, or other organisms, including other mammals, may be used to express humanized antibodies.

The above-described antibodies may be employed to isolate or to identify clones expressing the polypeptide or to purify the polypeptides by affinity chromatography. Antibodies  
5 against polypeptides of the present invention may also be employed to treat diseases of the invention, amongst others.

Polypeptides and polynucleotides of the present invention may also be used as vaccines. Accordingly, in a further aspect, the present invention relates to a method for inducing an immunological response in a mammal that comprises inoculating the mammal with a polypeptide  
10 of the present invention, adequate to produce antibody and/or T cell immune response, including, for example, cytokine-producing T cells or cytotoxic T cells, to protect said animal from disease, whether that disease is already established within the individual or not. An immunological response in a mammal may also be induced by a method comprises delivering a polypeptide of the present invention *via* a vector directing expression of the polynucleotide and coding for the polypeptide *in*  
15 *vivo* in order to induce such an immunological response to produce antibody to protect said animal from diseases of the invention. One way of administering the vector is by accelerating it into the desired cells as a coating on particles or otherwise. Such nucleic acid vector may comprise DNA, RNA, a modified nucleic acid, or a DNA/RNA hybrid. For use a vaccine, a polypeptide or a nucleic acid vector will be normally provided as a vaccine formulation (composition). The  
20 formulation may further comprise a suitable carrier. Since a polypeptide may be broken down in the stomach, it is preferably administered parenterally (for instance, subcutaneous, intra-muscular, intravenous, or intra-dermal injection). Formulations suitable for parenteral administration include aqueous and non-aqueous sterile injection solutions that may contain anti-oxidants, buffers, bacteriostats and solutes that render the formulation isotonic with the blood of the recipient; and  
25 aqueous and non-aqueous sterile suspensions that may include suspending agents or thickening agents. The formulations may be presented in unit-dose or multi-dose containers, for example, sealed ampoules and vials and may be stored in a freeze-dried condition requiring only the addition of the sterile liquid carrier immediately prior to use. The vaccine formulation may also include adjuvant systems for enhancing the immunogenicity of the formulation, such as oil-in water  
30 systems and other systems known in the art. The dosage will depend on the specific activity of the vaccine and can be readily determined by routine experimentation.

Polypeptides of the present invention have one or more biological functions that are of relevance in one or more disease states, in particular the diseases of the invention hereinbefore mentioned. It is therefore useful to identify compounds that stimulate or inhibit the function or  
35 level of the polypeptide. Accordingly, in a further aspect, the present invention provides for a

method of screening compounds to identify those that stimulate or inhibit the function or level of the polypeptide. Such methods identify agonists or antagonists that may be employed for therapeutic and prophylactic purposes for such diseases of the invention as hereinbefore mentioned. Compounds may be identified from a variety of sources, for example, cells, cell-free preparations, chemical libraries, collections of chemical compounds, and natural product mixtures. Such agonists or antagonists so-identified may be natural or modified substrates, ligands, receptors, enzymes, etc., as the case may be, of the polypeptide; a structural or functional mimetic thereof (see Coligan *et al.*, Current Protocols in Immunology 1(2):Chapter 5 (1991)) or a small molecule. Such small molecules preferably have a molecular weight below 2,000 daltons, more preferably between 300 and 1,000 daltons, and most preferably between 400 and 700 daltons. It is preferred that these small molecules are organic molecules.

The screening method may simply measure the binding of a candidate compound to the polypeptide, or to cells or membranes bearing the polypeptide, or a fusion protein thereof, by means of a label directly or indirectly associated with the candidate compound. Alternatively, the screening method may involve measuring or detecting (qualitatively or quantitatively) the competitive binding of a candidate compound to the polypeptide against a labeled competitor (*e.g.* agonist or antagonist). Further, these screening methods may test whether the candidate compound results in a signal generated by activation or inhibition of the polypeptide, using detection systems appropriate to the cells bearing the polypeptide. Inhibitors of activation are generally assayed in the presence of a known agonist and the effect on activation by the agonist by the presence of the candidate compound is observed. Further, the screening methods may simply comprise the steps of mixing a candidate compound with a solution containing a polypeptide of the present invention, to form a mixture, measuring an activity of the genes set forth in Table I in the mixture, and comparing activity of the mixture of the genes set forth in Table I to a control mixture which contains no candidate compound.

Polypeptides of the present invention may be employed in conventional low capacity screening methods and also in high-throughput screening (HTS) formats. Such HTS formats include not only the well-established use of 96- and, more recently, 384-well micotiter plates but also emerging methods such as the nanowell method described by Schullek *et al.*, Anal Biochem., 246, 20-29, (1997).

Fusion proteins, such as those made from Fc portion and polypeptide of the genes set forth in Table I, as hereinbefore described, can also be used for high-throughput screening assays to identify antagonists for the polypeptide of the present invention (see D. Bennett *et al.*, J Mol Recognition, 8:52-58 (1995); and K. Johanson *et al.*, J Biol Chem, 270(16):9459-9471 (1995)).

The polynucleotides, polypeptides and antibodies to the polypeptide of the present invention may also be used to configure screening methods for detecting the effect of added compounds on the production of mRNA and polypeptide in cells. For example, an ELISA assay may be constructed for measuring secreted or cell associated levels of polypeptide using  
5 monoclonal and polyclonal antibodies by standard methods known in the art. This can be used to discover agents that may inhibit or enhance the production of polypeptide (also called antagonist or agonist, respectively) from suitably manipulated cells or tissues.

A polypeptide of the present invention may be used to identify membrane bound or soluble receptors, if any, through standard receptor binding techniques known in the art. These include, but  
10 are not limited to, ligand binding and crosslinking assays in which the polypeptide is labeled with a radioactive isotope (for instance,  $^{125}\text{I}$ ), chemically modified (for instance, biotinylated), labeled with a rare earth element (for instance, europium), or fused to a peptide sequence suitable for detection or purification, and incubated with a source of the putative receptor (cells, cell membranes, cell supernatants, tissue extracts, bodily fluids). Other methods include biophysical  
15 techniques such as surface plasmon resonance and spectroscopy. These screening methods may also be used to identify agonists and antagonists of the polypeptide that compete with the binding of the polypeptide to its receptors, if any. Standard methods for conducting such assays are well understood in the art.

Examples of antagonists of polypeptides of the present invention include antibodies or, in  
20 some cases, oligonucleotides or proteins that are closely related to the ligands, substrates, receptors, enzymes, etc., as the case may be, of the polypeptide, e.g., a fragment of the ligands, substrates, receptors, enzymes, etc.; or a small molecule that binds to the polypeptide of the present invention but does not elicit a response, so that the activity of the polypeptide is prevented.

Screening methods may also involve the use of transgenic technology and the genes set  
25 forth in Table I. The art of constructing transgenic animals is well established. For example, the genes set forth in Table I may be introduced through microinjection into the male pronucleus of fertilized oocytes, retroviral transfer into pre- or post-implantation embryos, or injection of genetically modified, such as by electroporation, embryonic stem cells into host blastocysts. Particularly useful transgenic animals are so-called "knock-in" animals in which an animal gene is  
30 replaced by the human equivalent within the genome of that animal. Knock-in transgenic animals are useful in the drug discovery process, for target validation, where the compound is specific for the human target. Other useful transgenic animals are so-called "knock-out" animals in which the expression of the animal ortholog of a polypeptide of the present invention and encoded by an endogenous DNA sequence in a cell is partially or completely annulled. The gene knock-out may  
35 be targeted to specific cells or tissues, may occur only in certain cells or tissues as a consequence of

the limitations of the technology, or may occur in all, or substantially all, cells in the animal. Transgenic animal technology also offers a whole animal expression-cloning system in which introduced genes are expressed to give large amounts of polypeptides of the present invention

Screening kits for use in the above described methods form a further aspect of the present invention. Such screening kits comprise:

- (a) a polypeptide of the present invention;
- (b) a recombinant cell expressing a polypeptide of the present invention;
- (c) a cell membrane expressing a polypeptide of the present invention; or
- (d) an antibody to a polypeptide of the present invention;

which polypeptide is preferably that set forth in the Sequence Listing.

It will be appreciated that in any such kit, (a), (b), (c) or (d) may comprise a substantial component.

The polypeptides of the present invention can be formulated into pharmaceutical compositions and administered in the same manner as described for other polypeptides. See, e.g., International Patent Application, Publication No. WO90/02762. Generally, these compositions contain a therapeutically effective amount of a polypeptide of this invention and an acceptable pharmaceutical carrier. Suitable carriers are well known to those of skill in the art and include, for example, saline. Alternatively, such compositions may include conventional delivery systems into which polypeptide of the invention is incorporated. Optionally, these compositions may contain other active ingredients.

The polypeptides of this invention may be administered by any appropriate internal route, and may be repeated as needed, e.g., as frequently as one to three times daily for between 1 day to about three weeks to once per week or once biweekly. Alternatively, the peptide maybe altered to reduce charge density and thus allow oral bioavailability. The dose and duration of treatment relates to the relative duration of the molecules of the present invention in the human circulation, and can be adjusted by one of skill in the art depending upon the condition being treated and the general health of the patient.

As used herein, the term "pharmaceutical" includes veterinary applications of the invention. The term "therapeutically effective amount" refers to that amount of therapeutic agent, which is useful for alleviating a selected condition.

In a specific embodiment, nucleic acids comprising sequences encoding the instant polypeptides or functional derivatives thereof, are administered to treat, inhibit or prevent a disease or disorder associated with aberrant expression and/or activity of a polypeptide of the invention, by way of gene therapy. "Gene therapy" refers to therapy performed by the administration to a subject



of an expressed or expressible nucleic acid. In this embodiment of the invention, the nucleic acids produce their encoded protein that mediates a therapeutic effect.

Any of the methods for gene therapy available in the art can be used according to the present invention. Exemplary methods are described below.

For general reviews of the methods of gene therapy, see Goldspiel et al., *Clinical Pharmacy* 12:488-505 (1993); Wu and Wu, *Biotherapy* 3:87-95 (1991); Tolstoshev, *Ann. Rev. Pharmacol. Toxicol.* 32:573-596 (1993); Mulligan, *Science* 260:926-932 (1993); and Morgan and Anderson, *Ann. Rev. Biochem.* 62:191-217 (1993); May, *TIBTECH* 11(5):155-215 (1993). Methods commonly known in the art of recombinant DNA technology which can be used are described in Ausubel et al. (eds.), *Current Protocols in Molecular Biology*, John Wiley & Sons, NY (1993); and Kriegler, *Gene Transfer and Expression, A Laboratory Manual*, Stockton Press, NY (1990).

In a preferred aspect, the compound comprises nucleic acid sequences encoding a polypeptide, said nucleic acid sequences being part of expression vectors that express a polypeptide in a suitable host. In particular, such nucleic acid sequences have promoters operably linked to the polypeptide coding region, said promoter being inducible or constitutive, and, optionally, tissue-specific. In another particular embodiment, nucleic acid molecules are used in which the polypeptide coding sequences and any other desired sequences are flanked by regions that promote homologous recombination at a desired site in the genome, thus providing for intrachromosomal expression of the polypeptide-encoding nucleic acids (Koller and Smithies, *Proc. Natl. Acad. Sci. USA* 86:8932-8935 (1989); Zijlstra et al., *Nature* 342:435-438 (1989).

Delivery of the nucleic acids into a patient may be either direct, in which case the patient is directly exposed to the nucleic acid or nucleic acid-carrying vectors, or indirect, in which case, cells are first transformed with the nucleic acids in vitro, then transplanted into the patient. These two approaches are known, respectively, as in vivo or ex vivo gene therapy.

In a specific embodiment, the nucleic acid sequences are directly administered in vivo, where it is expressed to produce the encoded product. This can be accomplished by any of numerous methods known in the art, e.g., by constructing them as part of an appropriate nucleic acid expression vector and administering it so that they become intracellular, e.g., by infection using defective or attenuated retrovirals or other viral vectors (see U.S. Pat. No. 4,980,286), or by direct injection of naked DNA, or by use of microparticle bombardment (e.g., a gene gun; Biolistic, Dupont), or coating with lipids or cell-surface receptors or transfecting agents, encapsulation in liposomes, microparticles, or microcapsules, or by administering them in linkage to a peptide which is known to enter the nucleus, by administering it in linkage to a ligand subject to receptor-mediated endocytosis (see, e.g., Wu and Wu, *J. Biol. Chem.* 262:4429-4432 (1987)) (which can be used to target cell types specifically expressing the receptors), etc. In another embodiment, nucleic

acid-ligand complexes can be formed in which the ligand comprises a fusogenic viral peptide to disrupt endosomes, allowing the nucleic acid to avoid lysosomal degradation. In yet another embodiment, the nucleic acid can be targeted *in vivo* for cell specific uptake and expression, by targeting a specific receptor (see, e.g., PCT Publications WO 92/06180; WO 92/22635; WO92/20316; WO93/14188, WO 93/20221). Alternatively, the nucleic acid can be introduced intracellularly and incorporated within host cell DNA for expression, by homologous recombination (Koller and Smithies, *Proc. Natl. Acad. Sci. USA* 86:8932-8935 (1989); Zijlstra et al., *Nature* 342:435-438 (1989)).

In a specific embodiment, viral vectors that contain nucleic acid sequences encoding a polypeptide of the invention are used. For example, a retroviral vector can be used (see Miller et al., *Meth. Enzymol.* 217:581-599 (1993)). These retroviral vectors contain the components necessary for the correct packaging of the viral genome and integration into the host cell DNA. The nucleic acid sequences encoding the antibody to be used in gene therapy are cloned into one or more vectors, which facilitates delivery of the gene into a patient. More detail about retroviral vectors can be found in Boesen et al., *Biotherapy* 6:291-302 (1994), which describes the use of a retroviral vector to deliver the *mdr1* gene to hematopoietic stem cells in order to make the stem cells more resistant to chemotherapy. Other references illustrating the use of retroviral vectors in gene therapy are: Clowes et al., *J. Clin. Invest.* 93:644-651 (1994); Kiem et al., *Blood* 83:1467-1473 (1994); Salmons and Gunzberg, *Human Gene Therapy* 4:129-141 (1993); and Grossman and Wilson, *Curr. Opin. in Genetics and Devel.* 3:110-114 (1993).

Adenoviruses are other viral vectors that can be used in gene therapy. Adenoviruses are especially attractive vehicles for delivering genes to respiratory epithelia. Adenoviruses naturally infect respiratory epithelia where they cause a mild disease. Other targets for adenovirus-based delivery systems are liver, the central nervous system, endothelial cells, and muscle. Adenoviruses have the advantage of being capable of infecting non-dividing cells. Kozarsky and Wilson, *Current Opinion in Genetics and Development* 3:499-503 (1993) present a review of adenovirus-based gene therapy. Bout et al., *Human Gene Therapy* 5:3-10 (1994) demonstrated the use of adenovirus vectors to transfer genes to the respiratory epithelia of rhesus monkeys. Other instances of the use of adenoviruses in gene therapy can be found in Rosenfeld et al., *Science* 252:431-434 (1991); Rosenfeld et al., *Cell* 68:143-155 (1992); Mastrangeli et al., *J. Clin. Invest.* 91:225-234 (1993); PCT Publication WO94/12649; and Wang, et al., *Gene Therapy* 2:775-783 (1995). In a preferred embodiment, adenovirus vectors are used.

Adeno-associated virus (AAV) has also been proposed for use in gene therapy (Walsh et al., *Proc. Soc. Exp. Biol. Med.* 204:289-300 (1993); U.S. Pat. No. 5,436,146).

Another approach to gene therapy involves transferring a gene to cells in tissue culture by such methods as electroporation, lipofection, calcium phosphate mediated transfection, or viral infection. Usually, the method of transfer includes the transfer of a selectable marker to the cells. The cells are then placed under selection to isolate those cells that have taken up and are expressing the transferred gene. Those cells are then delivered to a patient.

In this embodiment, the nucleic acid is introduced into a cell prior to administration in vivo of the resulting recombinant cell. Such introduction can be carried out by any method known in the art, including but not limited to transfection, electroporation, microinjection, infection with a viral or bacteriophage vector containing the nucleic acid sequences, cell fusion, chromosome-mediated gene transfer, microcell-mediated gene transfer, spheroplast fusion, etc. Numerous techniques are known in the art for the introduction of foreign genes into cells (see, e.g., Loeffler and Behr, *Meth. Enzymol.* 217:599-618 (1993); Cohen et al., *Meth. Enzymol.* 217:618-644 (1993); Cline, *Pharmac. Ther.* 29:69-92m (1985) and may be used in accordance with the present invention, provided that the necessary developmental and physiological functions of the recipient cells are not disrupted. The technique should provide for the stable transfer of the nucleic acid to the cell, so that the nucleic acid is expressible by the cell and preferably heritable and expressible by its cell progeny.

The resulting recombinant cells can be delivered to a patient by various methods known in the art. Recombinant blood cells (e.g., hematopoietic stem or progenitor cells) are preferably administered intravenously. The amount of cells envisioned for use depends on the desired effect, patient state, etc., and can be determined by one skilled in the art.

Cells into which a nucleic acid can be introduced for purposes of gene therapy encompass any desired, available cell type, and include but are not limited to epithelial cells, endothelial cells, keratinocytes, fibroblasts, muscle cells, hepatocytes; blood cells such as Tlymphocytes, Blymphocytes, monocytes, macrophages, neutrophils, eosinophils, megakaryocytes, granulocytes; various stem or progenitor cells, in particular hematopoietic stem or progenitor cells, e.g., as obtained from bone marrow, umbilical cord blood, peripheral blood, fetal liver, etc.

In a preferred embodiment, the cell used for gene therapy is autologous to the patient.

In an embodiment in which recombinant cells are used in gene therapy, nucleic acid sequences encoding a polypeptide are introduced into the cells such that they are expressible by the cells or their progeny, and the recombinant cells are then administered in vivo for therapeutic effect. In a specific embodiment, stem or progenitor cells are used. Any stem and/or progenitor cells which can be isolated and maintained in vitro can potentially be used in accordance with this embodiment of the present invention (see e.g. PCT Publication WO 94/08598; Stemple and Anderson, *Cell* 71:973-985 (1992); Rheinwald, *Meth. Cell Bio.* 21A:229 (1980); and Pittelkow and Scott, *Mayo Clinic Proc.* 61:771 (1986)).

In a specific embodiment, the nucleic acid to be introduced for purposes of gene therapy comprises an inducible promoter operably linked to the coding region, such that expression of the nucleic acid is controllable by controlling the presence or absence of the appropriate inducer of transcription.

5           The invention provides methods of treatment, inhibition and prophylaxis by administration to a subject of an effective amount of a compound or pharmaceutical composition of the invention, preferably a polypeptide of the invention. In a preferred aspect, the compound is substantially purified (e.g., substantially free from substances that limit its effect or produce undesired side-effects). The subject is preferably an animal, including but not limited to animals such as cows,  
10       pigs, horses, chickens, cats, dogs, etc., and is preferably a mammal, and most preferably human.

Formulations and methods of administration that can be employed when the compound comprises a nucleic acid or a polypeptide are described above; additional appropriate formulations and routes of administration can be selected from among those described herein below.

Various delivery systems are known and can be used to administer a compound of the  
15       invention, e.g., encapsulation in liposomes, microparticles, microcapsules, recombinant cells capable of expressing the compound, receptor-mediated endocytosis (see, e.g., Wu and Wu, J. Biol. Chem. 262:4429-4432 (1987)), construction of a nucleic acid as part of a retroviral or other vector, etc. Methods of introduction include but are not limited to intradermal, intramuscular, intraperitoneal, intravenous, subcutaneous, intranasal, epidural, and oral routes. The compounds or  
20       compositions may be administered by any convenient route, for example by infusion or bolus injection, by absorption through epithelial or mucocutaneous linings (e.g., oral mucosa, rectal and intestinal mucosa, etc.) and may be administered together with other biologically active agents. Administration can be systemic or local. In addition, it may be desirable to introduce the pharmaceutical compounds or compositions of the invention into the central nervous system by any  
25       suitable route, including intraventricular and intrathecal injection; intraventricular injection may be facilitated by an intraventricular catheter, for example, attached to a reservoir, such as an Ommaya reservoir. Pulmonary administration can also be employed, e.g., by use of an inhaler or nebulizer, and formulation with an aerosolizing agent.

30           In a specific embodiment, it may be desirable to administer the pharmaceutical compounds or compositions of the invention locally to the area in need of treatment; this may be achieved by, for example, and not by way of limitation, local infusion during surgery, topical application, e.g., in conjunction with a wound dressing after surgery, by injection, by means of a catheter, by means of a suppository, or by means of an implant, said implant being of a porous, non-porous, or gelatinous material, including membranes, such as sialastic membranes, or fibers. Preferably, when

administering a protein, including an antibody, of the invention, care must be taken to use materials to which the protein does not absorb.

In another embodiment, the compound or composition can be delivered in a vesicle, in particular a liposome (see Langer, *Science* 249:1527-1533 (1990); Treat et al., in *Liposomes in the Therapy of Infectious Disease and Cancer*, Lopez-Berestein and Fidler (eds.), Liss, New York, pp. 353-365 (1989); Lopez-Berestein, *ibid.*, pp. 317-327; see generally *ibid.*)

In yet another embodiment, the compound or composition can be delivered in a controlled release system. In one embodiment, a pump may be used (see Langer, *supra*; Sefton, *CRC Crit. Ref. Biomed. Eng.* 14:201 (1987); Buchwald et al., *Surgery* 88:507 (1980); Saudek et al., *N. Engl. J. Med.* 321:574 (1989)). In another embodiment, polymeric materials can be used (see *Medical Applications of Controlled Release*, Langer and Wise (eds.), CRC Pres., Boca Raton, Fla. (1974); *Controlled Drug Bioavailability, Drug Product Design and Performance*, Smolen and Ball (eds.), Wiley, New York (1984); Ranger and Peppas, J., *Macromol. Sci. Rev. Macromol. Chem.* 23:61 (1983); see also Levy et al., *Science* 228:190 (1985); During et al., *Ann. Neurol.* 25:351 (1989); Howard et al., *J. Neurosurg.* 71:105 (1989)). In yet another embodiment, a controlled release system can be placed in proximity of the therapeutic target, i.e., the brain, thus requiring only a fraction of the systemic dose (see, e.g., Goodson, in *Medical Applications of Controlled Release*, *supra*, vol. 2, pp. 115-138 (1984)).

Other controlled release systems are discussed in the review by Langer (*Science* 249:1527-1533 (1990)).

In a specific embodiment where the compound of the invention is a nucleic acid encoding a polypeptide, the nucleic acid can be administered in vivo to promote expression of its encoded protein, by constructing it as part of an appropriate nucleic acid expression vector and administering it so that it becomes intracellular, e.g., by use of a retroviral vector (see U.S. Pat. No. 4,980,286), or by direct injection, or by use of microparticle bombardment (e.g., a gene gun; Biolistic, Dupont), or coating with lipids or cell-surface receptors or transfecting agents, or by administering it in linkage to a homeobox-like peptide which is known to enter the nucleus (see e.g., Joliet et al., *Proc. Natl. Acad. Sci. USA* 88:1864-1868 (1991)), etc. Alternatively, a nucleic acid can be introduced intracellularly and incorporated within host cell DNA for expression, by homologous recombination.

The present invention also provides pharmaceutical compositions. Such compositions comprise a therapeutically effective amount of a compound, and a pharmaceutically acceptable carrier. In a specific embodiment, the term "pharmaceutically acceptable" means approved by a regulatory agency of the Federal or a state government or listed in the U.S. Pharmacopeia or other generally recognized pharmacopeia for use in animals, and more particularly in humans. The term

"carrier" refers to a diluent, adjuvant, excipient, or vehicle with which the therapeutic is administered. Such pharmaceutical carriers can be sterile liquids, such as water and oils, including those of petroleum, animal, vegetable or synthetic origin, such as peanut oil, soybean oil, mineral oil, sesame oil and the like. Water is a preferred carrier when the pharmaceutical composition is administered intravenously. Saline solutions and aqueous dextrose and glycerol solutions can also be employed as liquid carriers, particularly for injectable solutions. Suitable pharmaceutical excipients include starch, glucose, lactose, sucrose, gelatin, malt, rice, flour, chalk, silica gel, sodium stearate, glycerol monostearate, talc, sodium chloride, dried skim milk, glycerol, propylene, glycol, water, ethanol and the like. The composition, if desired, can also contain minor amounts of wetting or emulsifying agents, or pH buffering agents. These compositions can take the form of solutions, suspensions, emulsion, tablets, pills, capsules, powders, sustained-release formulations and the like. The composition can be formulated as a suppository, with traditional binders and carriers such as triglycerides. Oral formulation can include standard carriers such as pharmaceutical grades of mannitol, lactose, starch, magnesium stearate, sodium saccharine, cellulose, magnesium carbonate, etc. Examples of suitable pharmaceutical carriers are described in "Remington's Pharmaceutical Sciences" by E. W. Martin. Such compositions will contain a therapeutically effective amount of the compound, preferably in purified form, together with a suitable amount of carrier so as to provide the form for proper administration to the patient. The formulation should suit the mode of administration.

In a preferred embodiment, the composition is formulated in accordance with routine procedures as a pharmaceutical composition adapted for intravenous administration to human beings. Typically, compositions for intravenous administration are solutions in sterile isotonic aqueous buffer. Where necessary, the composition may also include a solubilizing agent and a local anesthetic such as lignocaine to ease pain at the site of the injection. Generally, the ingredients are supplied either separately or mixed together in unit dosage form, for example, as a dry lyophilized powder or water free concentrate in a hermetically sealed container such as an ampoule or sachette indicating the quantity of active agent. Where the composition is to be administered by infusion, it can be dispensed with an infusion bottle containing sterile pharmaceutical grade water or saline. Where the composition is administered by injection, an ampoule of sterile water for injection or saline can be provided so that the ingredients may be mixed prior to administration.

The compounds of the invention can be formulated as neutral or salt forms. Pharmaceutically acceptable salts include those formed with anions such as those derived from hydrochloric, phosphoric, acetic, oxalic, tartaric acids, etc., and those formed with cations such as those derived from sodium, potassium, ammonium, calcium, ferric hydroxides, isopropylamine, triethylamine, 2-ethylamino ethanol, histidine, procaine, etc.

The amount of the compound of the invention which will be effective in the treatment, inhibition and prevention of a disease or disorder associated with aberrant expression and/or activity of a polypeptide of the invention can be determined by standard clinical techniques. In addition, in vitro assays may optionally be employed to help identify optimal dosage ranges. The precise dose to be employed in the formulation will also depend on the route of administration, and the seriousness of the disease or disorder, and should be decided according to the judgment of the practitioner and each patient's circumstances. Effective doses may be extrapolated from dose-response curves derived from in vitro or animal model test systems.

For polypeptides, the dosage administered to a patient is typically 0.1 mg/kg to 100 mg/kg of the patient's body weight. Preferably, the dosage administered to a patient is between 0.1 mg/kg and 20 mg/kg of the patient's body weight, more preferably 1 mg/kg to 10 mg/kg of the patient's body weight. Generally, human polypeptides have a longer half-life within the human body than polypeptides from other species due to the immune response to the foreign polypeptides. Thus, lower dosages of human polypeptides and less frequent administration is often possible. Further, the dosage and frequency of administration of polypeptides of the invention may be reduced by enhancing uptake and tissue penetration (e.g., into the brain) of the polypeptides by modifications such as, for example, lipidation.

The invention also provides a pharmaceutical pack or kit comprising one or more containers filled with one or more of the ingredients of the pharmaceutical compositions of the invention. Optionally associated with such container(s) can be a notice in the form prescribed by a governmental agency regulating the manufacture, use or sale of pharmaceuticals or biological products, which notice reflects approval by the agency of manufacture, use or sale for human administration.

This invention provides for a pharmaceutical composition which comprises a polypeptide of this invention and a pharmaceutically acceptable carrier, diluent or excipient. Accordingly, the polypeptide may be used in the manufacture of a medicament. Pharmaceutical compositions of the invention may be formulated as solutions or lyophilized powders for parenteral administration. Powders may be reconstituted by addition of a suitable diluent or other pharmaceutically acceptable carrier prior to use. The liquid formulation may be a buffered, isotonic, aqueous solution.

Examples of suitable diluents are normal isotonic saline solution, standard 5% dextrose in water or buffered sodium or ammonium acetate solution. Such formulation is especially suitable for parenteral administration, but may also be used for oral administration or contained in a metered dose inhaler or nebulizer for insufflation. It may be desirable to add excipients such as polyvinylpyrrolidone, gelatin, hydroxy cellulose, acacia, polyethylene glycol, mannitol, sodium chloride or sodium citrate.

Alternately, the polypeptide may be encapsulated, tableted or prepared in an emulsion or syrup for oral administration. Pharmaceutically acceptable solid or liquid carriers may be added to enhance or stabilize the composition, or to facilitate preparation of the composition. Solid carriers include starch, lactose, calcium sulfate dihydrate, terra alba, magnesium stearate or stearic acid, talc, pectin, acacia, agar or gelatin. Liquid carriers include syrup, peanut oil, olive oil, saline and water. The carrier may also include a sustained release material such as glyceryl monostearate or glyceryl distearate, alone or with a wax. The amount of solid carrier varies but, preferably, will be between about 20 mg to about 1 g per dosage unit. The pharmaceutical preparations are made following the conventional techniques of pharmacy involving milling, mixing, granulating, and compressing, when necessary, for tablet forms; or milling, mixing and filling for hard gelatin capsule forms. When a liquid carrier is used, the preparation will be in the form of a syrup, elixir, emulsion or an aqueous or non-aqueous suspension. Such a liquid formulation may be administered directly p.o. or filled into a soft gelatin capsule.

The mode of administration of a polypeptide of the invention may be any suitable route which delivers the agent to the host. The polypeptides and pharmaceutical compositions of the invention are particularly useful for parenteral administration, i.e., subcutaneously, intramuscularly, intravenously or intranasally.

Polypeptide of the invention may be prepared as pharmaceutical compositions containing an effective amount of a polypeptide of the invention as an active ingredient in a pharmaceutically acceptable carrier. In the compositions of the invention, an aqueous suspension or solution containing the polypeptide, preferably buffered at physiological pH, in a form ready for injection is preferred. The compositions for parenteral administration will commonly comprise a solution of the polypeptide of the invention or a cocktail thereof dissolved in an pharmaceutically acceptable carrier, preferably an aqueous carrier. A variety of aqueous carriers may be employed, e.g., 0.4% saline, 0.3% glycine and the like. These solutions are sterile and generally free of particulate matter. These solutions may be sterilized by conventional, well known sterilization techniques (e.g., filtration). The compositions may contain pharmaceutically acceptable auxiliary substances as required to approximate physiological conditions such as pH adjusting and buffering agents, etc. The concentration of the polypeptide of the invention in such pharmaceutical formulation can vary widely, i.e., from less than about 0.5%, usually at or at least about 1% to as much as 15 or 20% by weight and will be selected primarily based on fluid volumes, viscosities, etc., according to the particular mode of administration selected.

Thus, a pharmaceutical composition of the invention for intramuscular injection could be prepared to contain 1 mL sterile buffered water, and between about 1 ng to about 100 mg, e.g. about 50 ng to about 30 mg or more preferably, about 5 mg to about 25 mg, of a polypeptide of the



invention. Similarly, a pharmaceutical composition of the invention for intravenous infusion could be made up to contain about 250 mL of sterile Ringer's solution, and about 1 mg to about 30 mg and preferably 5 mg to about 25 mg of a polypeptide of the invention. Actual methods for preparing parenterally administrable compositions are well known or will be apparent to those skilled in the art and are described in more detail in, for example, "Remington's Pharmaceutical Science", 15th ed., Mack Publishing Company, Easton, Pennsylvania.

It is preferred that the polypeptide of the invention, when in a pharmaceutical preparation, be present in unit dose forms. The appropriate therapeutically effective dose can be determined readily by those of skill in the art. Such dose may, if necessary, be repeated at appropriate time intervals selected as appropriate by a physician during the response period.

The present invention may be embodied in other specific forms, without departing from the spirit or essential attributes thereof, and, accordingly, reference should be made to the appended claims, rather than to the foregoing specification or following examples, as indicating the scope of the invention.

## Glossary

The following definitions are provided to facilitate understanding of certain terms used frequently hereinbefore.

"Antibodies" as used herein includes polyclonal and monoclonal antibodies, chimeric, single chain, and humanized antibodies and fully human antibodies produced in transgeneic mice, where the mouse antibody coding genes have been suppressed or replaced and substituted with human antibody coding genes, as well as Fab fragments, including the products of an Fab or other immunoglobulin expression library.

"Isolated" means altered "by the hand of man" from its natural state, *i.e.*, if it occurs in nature, it has been changed or removed from its original environment, or both. For example, a polynucleotide or a polypeptide naturally present in a living organism is not "isolated," but the same polynucleotide or polypeptide separated from the coexisting materials of its natural state is "isolated", as the term is employed herein. Moreover, a polynucleotide or polypeptide that is introduced into an organism by transformation, genetic manipulation or by any other recombinant method is "isolated" even if it is still present in said organism, which organism may be living or non-living.

"Secreted protein activity or secreted polypeptide activity" or "biological activity of the secreted protein or secreted polypeptide" refers to the metabolic or physiologic function of said secreted protein including similar activities or improved activities or these activities with decreased

undesirable side-effects. Also included are antigenic and immunogenic activities of said secreted protein.

"Secreted protein gene" refers to a polynucleotide comprising any of the attached nucleotide sequences or allelic variants thereof and/or their complements.

5 "Polynucleotide" generally refers to any polyribonucleotide (RNA) or polydeoxribonucleotide (DNA), which may be unmodified or modified RNA or DNA.

"Polynucleotides" include, without limitation, single- and double-stranded DNA, DNA that is a mixture of single- and double-stranded regions, single- and double-stranded RNA, and RNA that is a mixture of single- and double-stranded regions, hybrid molecules comprising DNA and RNA that  
10 may be single-stranded or, more typically, double-stranded or a mixture of single- and double-stranded regions. In addition, "polynucleotide" refers to triple-stranded regions comprising RNA or DNA or both RNA and DNA. The term "polynucleotide" also includes DNAs or RNAs containing one or more modified bases and DNAs or RNAs with backbones modified for stability or for other reasons. "Modified" bases include, for example, tritylated bases and unusual bases  
15 such as inosine. A variety of modifications may be made to DNA and RNA; thus, "polynucleotide" embraces chemically, enzymatically or metabolically modified forms of polynucleotides as typically found in nature, as well as the chemical forms of DNA and RNA characteristic of viruses and cells. "Polynucleotide" also embraces relatively short polynucleotides, often referred to as oligonucleotides.

20 "Polypeptide" refers to any polypeptide comprising two or more amino acids joined to each other by peptide bonds or modified peptide bonds, i.e., peptide isosteres. "Polypeptide" refers to both short chains, commonly referred to as peptides, oligopeptides or oligomers, and to longer chains, generally referred to as proteins. Polypeptides may contain amino acids other than the 20 gene-encoded amino acids. "Polypeptides" include amino acid sequences modified either by  
25 natural processes, such as post-translational processing, or by chemical modification techniques that are well known in the art. Such modifications are well described in basic texts and in more detailed monographs, as well as in a voluminous research literature. Modifications may occur anywhere in a polypeptide, including the peptide backbone, the amino acid side-chains and the amino or carboxyl termini. It will be appreciated that the same type of modification may be present  
30 to the same or varying degrees at several sites in a given polypeptide. Also, a given polypeptide may contain many types of modifications. Polypeptides may be branched as a result of ubiquitination, and they may be cyclic, with or without branching. Cyclic, branched and branched cyclic polypeptides may result from post-translation natural processes or may be made by synthetic methods. Modifications include acetylation, acylation, ADP-ribosylation, amidation, biotinylation,  
35 covalent attachment of flavin, covalent attachment of a heme moiety, covalent attachment of a

nucleotide or nucleotide derivative, covalent attachment of a lipid or lipid derivative, covalent attachment of phosphatidylinositol, cross-linking, cyclization, disulfide bond formation, demethylation, formation of covalent cross-links, formation of cystine, formation of pyroglutamate, formylation, gamma-carboxylation, glycosylation, GPI anchor formation, hydroxylation, iodination, methylation, myristoylation, oxidation, proteolytic processing, phosphorylation, prenylation, racemization, selenoylation, sulfation, transfer-RNA mediated addition of amino acids to proteins such as arginylation, and ubiquitination (see, for instance, *Proteins - Structure and Molecular Properties*, 2nd Ed., T. E. Creighton, W. H. Freeman and Company, New York, 1993; Wold, F., *Post-translational Protein Modifications: Perspectives and Prospects*, 1-12, in *Post-translational Covalent Modification of Proteins*, B. C. Johnson, Ed., Academic Press, New York, 1983; Seifter *et al.*, "Analysis for protein modifications and nonprotein cofactors", *Meth Enzymol*, 182, 626-646, 1990, and Rattan *et al.*, "Protein Synthesis: Post-translational Modifications and Aging", *Ann NY Acad Sci*, 663, 48-62, 1992).

"Fragment" of a polypeptide sequence refers to a polypeptide sequence that is shorter than the reference sequence but that retains essentially the same biological function or activity as the reference polypeptide. "Fragment" of a polynucleotide sequence refers to a polynucleotide sequence that is shorter than the reference sequence set forth in the Sequence Listing.

"Variant" refers to a polynucleotide or polypeptide that differs from a reference polynucleotide or polypeptide, but retains the essential properties thereof. A typical variant of a polynucleotide differs in nucleotide sequence from the reference polynucleotide. Changes in the nucleotide sequence of the variant may or may not alter the amino acid sequence of a polypeptide encoded by the reference polynucleotide. Nucleotide changes may result in amino acid substitutions, additions, deletions, fusions and truncations in the polypeptide encoded by the reference sequence, as discussed below. A typical variant of a polypeptide differs in amino acid sequence from the reference polypeptide. Generally, alterations are limited so that the sequences of the reference polypeptide and the variant are closely similar overall and, in many regions, identical. A variant and reference polypeptide may differ in amino acid sequence by one or more substitutions, insertions, deletions in any combination. A substituted or inserted amino acid residue may or may not be one encoded by the genetic code. Typical conservative substitutions include Gly, Ala; Val, Ile, Leu; Asp, Glu; Asn, Gln; Ser, Thr; Lys, Arg; and Phe and Tyr. A variant of a polynucleotide or polypeptide may be naturally occurring such as an allele, or it may be a variant that is not known to occur naturally. Non-naturally occurring variants of polynucleotides and polypeptides may be made by mutagenesis techniques or by direct synthesis. Also included as variants are polypeptides having one or more post-translational modifications, for instance glycosylation, phosphorylation, methylation, ADP ribosylation and the like. Embodiments include

methylation of the N-terminal amino acid, phosphorylations of serines and threonines and modification of C-terminal glycines.

"Allele" refers to one of two or more alternative forms of a gene occurring at a given locus in the genome.

5 "Polymorphism" refers to a variation in nucleotide sequence (and encoded polypeptide sequence, if relevant) at a given position in the genome within a population.

"Single Nucleotide Polymorphism" (SNP) refers to the occurrence of nucleotide variability at a single nucleotide position in the genome, within a population. An SNP may occur within a gene or within intergenic regions of the genome. SNPs can be assayed using Allele Specific  
10 Amplification (ASA). For the process at least 3 primers are required. A common primer is used in reverse complement to the polymorphism being assayed. This common primer can be between 50 and 1500 bps from the polymorphic base. The other two (or more) primers are identical to each other except that the final 3' base wobbles to match one of the two (or more) alleles that make up the polymorphism. Two (or more) PCR reactions are then conducted on sample DNA, each using  
15 the common primer and one of the Allele Specific Primers.

"Splice Variant" as used herein refers to cDNA molecules produced from RNA molecules initially transcribed from the same genomic DNA sequence but which have undergone alternative RNA splicing. Alternative RNA splicing occurs when a primary RNA transcript undergoes  
20 splicing, generally for the removal of introns, which results in the production of more than one mRNA molecule each of that may encode different amino acid sequences. The term splice variant also refers to the proteins encoded by the above cDNA molecules.

"Identity" reflects a relationship between two or more polypeptide sequences or two or more polynucleotide sequences, determined by comparing the sequences. In general, identity refers to an exact nucleotide to nucleotide or amino acid to amino acid correspondence of the two  
25 polynucleotide or two polypeptide sequences, respectively, over the length of the sequences being compared.

"% Identity" - For sequences where there is not an exact correspondence, a "% identity" may be determined. In general, the two sequences to be compared are aligned to give a maximum correlation between the sequences. This may include inserting "gaps" in either one or both  
30 sequences, to enhance the degree of alignment. A % identity may be determined over the whole length of each of the sequences being compared (so-called global alignment), that is particularly suitable for sequences of the same or very similar length, or over shorter, defined lengths (so-called local alignment), that is more suitable for sequences of unequal length.

"Similarity" is a further, more sophisticated measure of the relationship between two  
35 polypeptide sequences. In general, "similarity" means a comparison between the amino acids of

two polypeptide chains, on a residue by residue basis, taking into account not only exact correspondences between a between pairs of residues, one from each of the sequences being compared (as for identity) but also, where there is not an exact correspondence, whether, on an evolutionary basis, one residue is a likely substitute for the other. This likelihood has an associated  
 5 "score" from which the "% similarity" of the two sequences can then be determined.

Methods for comparing the identity and similarity of two or more sequences are well known in the art. Thus for instance, programs available in the Wisconsin Sequence Analysis Package, version 9.1 (Devereux J et al, Nucleic Acids Res, 12, 387-395, 1984, available from Genetics Computer Group, Madison, Wisconsin, USA), for example the programs BESTFIT and  
 10 GAP, may be used to determine the % identity between two polynucleotides and the % identity and the % similarity between two polypeptide sequences. BESTFIT uses the "local homology" algorithm of Smith and Waterman (J Mol Biol, 147,195-197, 1981, Advances in Applied Mathematics, 2, 482-489, 1981) and finds the best single region of similarity between two sequences. BESTFIT is more suited to comparing two polynucleotide or two polypeptide  
 15 sequences that are dissimilar in length, the program assuming that the shorter sequence represents a portion of the longer. In comparison, GAP aligns two sequences, finding a "maximum similarity", according to the algorithm of Neddleman and Wunsch (J Mol Biol, 48, 443-453, 1970). GAP is more suited to comparing sequences that are approximately the same length and an alignment is expected over the entire length. Preferably, the parameters "Gap Weight" and "Length Weight"  
 20 used in each program are 50 and 3, for polynucleotide sequences and 12 and 4 for polypeptide sequences, respectively. Preferably, % identities and similarities are determined when the two sequences being compared are optimally aligned.

Other programs for determining identity and/or similarity between sequences are also known in the art, for instance the BLAST family of programs (Altschul S F et al, J Mol Biol, 215,  
 25 403-410, 1990, Altschul S F et al, Nucleic Acids Res., 25:389-3402, 1997, available from the National Center for Biotechnology Information (NCBI), Bethesda, Maryland, USA and accessible through the home page of the NCBI at [www.ncbi.nlm.nih.gov](http://www.ncbi.nlm.nih.gov)) and FASTA (Pearson W R, Methods in Enzymology, 183, 63-99, 1990; Pearson W R and Lipman D J, Proc Nat Acad Sci USA, 85, 2444-2448,1988, available as part of the Wisconsin Sequence Analysis Package).

30 Preferably, the BLOSUM62 amino acid substitution matrix (Henikoff S and Henikoff J G, Proc. Nat. Acad Sci. USA, 89, 10915-10919, 1992) is used in polypeptide sequence comparisons including where nucleotide sequences are first translated into amino acid sequences before comparison.

Preferably, the program BESTFIT is used to determine the % identity of a query  
 35 polynucleotide or a polypeptide sequence with respect to a reference polynucleotide or a

polypeptide sequence, the query and the reference sequence being optimally aligned and the parameters of the program set at the default value, as hereinbefore described.

"Identity Index" is a measure of sequence relatedness which may be used to compare a candidate sequence (polynucleotide or polypeptide) and a reference sequence. Thus, for instance, a candidate polynucleotide sequence having, for example, an Identity Index of 0.95 compared to a reference polynucleotide sequence is identical to the reference sequence except that the candidate polynucleotide sequence may include on average up to five differences per each 100 nucleotides of the reference sequence. Such differences are selected from the group consisting of at least one nucleotide deletion, substitution, including transition and transversion, or insertion. These differences may occur at the 5' or 3' terminal positions of the reference polynucleotide sequence or anywhere between these terminal positions, interspersed either individually among the nucleotides in the reference sequence or in one or more contiguous groups within the reference sequence. In other words, to obtain a polynucleotide sequence having an Identity Index of 0.95 compared to a reference polynucleotide sequence, an average of up to 5 in every 100 of the nucleotides of the in the reference sequence may be deleted, substituted or inserted, or any combination thereof, as hereinbefore described. The same applies *mutatis mutandis* for other values of the Identity Index, for instance 0.96, 0.97, 0.98 and 0.99.

Similarly, for a polypeptide, a candidate polypeptide sequence having, for example, an Identity Index of 0.95 compared to a reference polypeptide sequence is identical to the reference sequence except that the polypeptide sequence may include an average of up to five differences per each 100 amino acids of the reference sequence. Such differences are selected from the group consisting of at least one amino acid deletion, substitution, including conservative and non-conservative substitution, or insertion. These differences may occur at the amino- or carboxy-terminal positions of the reference polypeptide sequence or anywhere between these terminal positions, interspersed either individually among the amino acids in the reference sequence or in one or more contiguous groups within the reference sequence. In other words, to obtain a polypeptide sequence having an Identity Index of 0.95 compared to a reference polypeptide sequence, an average of up to 5 in every 100 of the amino acids in the reference sequence may be deleted, substituted or inserted, or any combination thereof, as hereinbefore described. The same applies *mutatis mutandis* for other values of the Identity Index, for instance 0.96, 0.97, 0.98 and 0.99.

The relationship between the number of nucleotide or amino acid differences and the Identity Index may be expressed in the following equation:

$$n_a \leq x_a - (x_a \cdot I),$$

in which:

$n_a$  is the number of nucleotide or amino acid differences,

$x_a$  is the total number of nucleotides or amino acids in a sequence set forth in the Sequence Listing,

I is the Identity Index,

5 • is the symbol for the multiplication operator, and

in which any non-integer product of  $x_a$  and I is rounded down to the nearest integer prior to subtracting it from  $x_a$ .

"Homolog" is a generic term used in the art to indicate a polynucleotide or polypeptide sequence possessing a high degree of sequence relatedness to a reference sequence. Such relatedness may be quantified by determining the degree of identity and/or similarity between the two sequences as hereinbefore defined. Falling within this generic term are the terms "ortholog", and "paralog". "Ortholog" refers to a polynucleotide or polypeptide that is the functional equivalent of the polynucleotide or polypeptide in another species. "Paralog" refers to a polynucleotide or polypeptide that within the same species which is functionally similar.

15 "Fusion protein" refers to a protein encoded by two, often unrelated, fused genes or fragments thereof. In one example, EP-A-0 464 533-A discloses fusion proteins comprising various portions of constant region of immunoglobulin molecules together with another human protein or part thereof. In many cases, employing an immunoglobulin Fc region as a part of a fusion protein is advantageous for use in therapy and diagnosis resulting in, for example, improved pharmacokinetic properties [see, *e.g.*, EP-A 0232 262]. On the other hand, for some uses it would be desirable to be able to delete the Fc part after the fusion protein has been expressed, detected and purified.

25 All publications and references, including but not limited to patents and patent applications, cited in this specification are herein incorporated by reference in their entirety as if each individual publication or reference were specifically and individually indicated to be incorporated by reference herein as being fully set forth. Any patent application to which this application claims priority is also incorporated by reference herein in its entirety in the manner described above for publications and references.

**Table I.**

Gene Name	GSK Gene ID	Nucleic Acid SEQ ID NO's	Corresponding Protein SEQ ID NO's
sbg237163LIPASE	237163	SEQ ID NO:1	SEQ ID NO:23
sbg251170CEAa	251170	SEQ ID NO:2 SEQ ID NO:3	SEQ ID NO:24 SEQ ID NO:25
sbg389686WNT15a	389686	SEQ ID NO:4	SEQ ID NO:26

		SEQ ID NO:5	SEQ ID NO:27
sbg236015LIPASE	236015	SEQ ID NO:6 SEQ ID NO:7	SEQ ID NO:28 SEQ ID NO:29
sbg417005LAMININ_ALPHA	417005	SEQ ID NO:8 SEQ ID NO:9	SEQ ID NO:30 SEQ ID NO:31
sbg425649KINASEa	425649	SEQ ID NO:10	SEQ ID NO:32
sbg419582PROTOCADHERIN	419582	SEQ ID NO:11 SEQ ID NO:12	SEQ ID NO:33 SEQ ID NO:34
sbg453915TECTORINa	453915	SEQ ID NO:13	SEQ ID NO:35
SBh385630.antiinflam	385630	SEQ ID NO:14 SEQ ID NO:15	SEQ ID NO:36 SEQ ID NO:37
sbg471005nAChR	471005	SEQ ID NO:16	SEQ ID NO:38
sbg442445PROa	442445	SEQ ID NO:17	SEQ ID NO:39
sbg456548CytoRa	456548	SEQ ID NO:18 SEQ ID NO:19	SEQ ID NO:40 SEQ ID NO:41
sbg456548CytoRa	456548b	SEQ ID NO:20	SEQ ID NO:42
sbg442358PROa	442358	SEQ ID NO:21 SEQ ID NO:22	SEQ ID NO:43 SEQ ID NO:44



Table II

Gene Name	Gene Family	Closest Polynucleotide by homology	Closest Polypeptide by homology	Cell Localization (by homology)
sbg237163 LIPASE	Pancreatic lipase	GB:AC011328 Direct submitted (06-OCT-1999) Genome Therapeutics Corporation, 100 Beaver Street, Waltham, MA 02453, USA	Mouse pancreatic lipase related protein 1, gi: 9256628 Remington, S.G., Lima, P.H. and Nelson, J.D. Invest. Ophthalmol. Vis. Sci. 40 (6), 1081-1090 (1999)	Secreted
sbg251170C EAa	Carcinoembryonic antigen	GB:AC020914 Submitted (12-JAN-2000) Production Sequencing Facility, DOE Joint Genome Institute, 2800 Mitchell Drive, Walnut Creek, CA 94598, USA	Mouse putative protein, gi: 12842545 Carninci, P., Shibata, Y., Hayatsu, N., Sugahara, Y., Shibata, K., Itoh, M., Konno, H., Okazaki, Y., Muramatsu, M. and Hayashizaki, Y. Genome Res. 10 (10), 1617-1630 (2000).	Secreted
sbg389686 WNT15a	WNT15	GB:AC015855 Directly submitted (17-NOV-1999) Whitehead Institute/MIT Center for Genome Research, 320 Charles Street, Cambridge, MA 02141, USA.	Chicken WNT14 protein, gi: 3915306 Bergstein I, Eisenberg LM, Bhalerao J, Jenkins NA, Copeland NG, Osborne MP, Bowcock AM, Brown AM; 1997; Genomics 46:450-8.	Secreted
sbg236015L IPASE	Lysosomal acid lipase	GB:AL358532 Directly submitted (15-DEC-2000) by Sanger Centre, Hinxton, Cambridgeshire, CB10 1SA, UK.	Rat lingual lipase, gi: 126307 Docherty, A.J., Bodmer, M.W., Angal, S., Verger, R., Riviere, C., Lowe, P.A., Lyons, A., Emtage, J.S. and Harris, T.J. Nucleic Acids Res. 13 (6), 1891-1903 (1985)	Secreted
sbg417005L AMININ_ALPHA	Laminin alpha	GB:AL354836 Direct submitted (02-MAY-2000) Sanger Centre, Hinxton, Cambridgeshire, CB10 1SA	Human laminin alpha 5, gi: 12274842 Submitted (14-FEB-2001) by Sanger Centre, Hinxton, Cambridgeshire, CB10 1SA, UK.	Secreted
sbg425649K INASEa	C casein kinase I-alpha	GB:AL356107 Submitted (16-MAY-2000) by Sanger Centre, Hinxton, Cambridgeshire, CB10 1SA, UK.	Human casein kinase I-alpha, gi: 2134872 Fish, K.J., Cegielska, A., Getman, M.E., Landes, G.M. and Virshup, D.M. J. Biol. Chem. 270 (25), 14875-14883 (1995)	Cytosolic

sbg419582P ROTOCAD HERIN	Protocadherin	GB:AL355593 Direct submitted (17-MAY-2000) Sanger Centre, Hinxton, Cambridgeshire, CB10 1SA, UK.	Human protocadherin 68 gi:11433373 Submitted (16-NOV-2000) by National Center for Biotechnology Information, NIH, Bethesda, MD 20894, USA	Secreted
sbg453915T ECTORINa	Tectorin Beta	SC:AL157786 Submitted (04-MAY-2001) by Sanger Centre, Hinxton, Cambridgeshire, CB10 1SA, UK.	Mouse tectorin beta, gi:7363457 Legan,P.K., Rau,A., Keen,J.N. and Richardson,G.P. J. Biol. Chem. 272 (13), 8791-8801 (1997)	Secreted
SBh385630. antiinflam	Lipase	GB:AC015525 Submitted (16-NOV-1999) by Whitehead Institute/MIT Center for Genome Research, 320 Charles Street, Cambridge, MA 02141, USA	Rabbit lacrimal lipase, gi:13560884 Submitted (20-FEB-2001) Ophthalmology, Regions Hospital, 640 Jackson Street, St. Paul, MN 55101, USA	Secreted

Table II (cont).

Gene Name	Gene Family	Closest Polynucleotide by homology	Closest Polypeptide by homology	Cell Localization (by homology)
sbg47100 5nAChR	Nicotinic acetylcholine receptor	GB:AC060812 Direct submitted (20-APR-2000) Whitehead Institute/MIT Center for Genome Research, 320 Charles Street, Cambridge, MA 02141, USA	Human cholinergic receptor, nicotinic, alpha polypeptide 10, gi:11138123 Lustig,L.R., Peng,H., Hiel,H., Yamamoto,T. and Fuchs,P.A. Genomics 73 (3), 272-283 (2001)	Membrane-bound
sbg44244 5PROa	Leucine rich repeat protein	GB:AC060234 Submitted (20-APR-2000) Genome Therapeutics Corporation, 100 Beaver Street, Waltham, MA 02453, USA	RIKEN cDNA mouse 4930442L21 gene Carninci,P., Shibata,Y., Hayatsu,N., Sugahara,Y., Shibata,K., Itoh,M., Konno,H., Okazaki,Y., Muramatsu,M. and Hayashizaki,Y. Genome Res. 10 (10), 1617-1630 (2000)	Cytosolic
sbg45654 8CytoRa	Cytokine receptor	GB:AL158138 Submitted (20-JAN-2001) by Sanger Centre, Hinxton, Cambridgeshire, CB10 1SA, UK.	Human IL20 receptor, gi:7657691 Xie MH, Aggarwal S, Ho WH, Foster J, Zhang Z, Stinson J, Wood WI, Goddard AD and Gurney AL. J. Biol. Chem. 275 (40), 31335-31339 (2000)	Membrane-bound
sbg44235 8PROa	Leucine rich repeat protein	GB:AL139099 Submitted (23-MAY-2000) by Genoscope - Centre National de Sequencage : BP 191 91006 EVRY cedex - FRANCE	Human EXMAD-9 gene seq: AAB27231 Submitted by INCYTE GENOMICS INC Application and publication date: WO200068380-A2, 16-NOV-00	Membrane-bound

Table III

Gene Name	Uses	Ass ciated Diseases
sbg237163 LIPASE	An embodiment of the invention is the use of sbg237163 LIPASE as replacement enzymes for patients with chronic pancreatitis. A close homologue of sbg237163 LIPASE is pancreatic lipase. Pancreatic lipase hydrolyzes dietary long chain triacylglycerol to free fatty acids and monoacylglycerols in the intestinal lumen (Lowe ME, Rosenblum JL, and Strauss AW; 1989; J Biol Chem 264:20042-8). Pancreatic steatorrhea and pancreatic diabetes are the dominant symptoms of patients in a certain stage of chronic pancreatitis. In this stage, the nutritional state is greatly disturbed and hypoglycemia and labile infection are involved. Pancreatic enzyme replacement therapy is the principal treatment method for pancreatic steatorrhea (Nakamura T, Takeuchi T, and Tando Y; 1998; Pancreas 16:329-36).	Cancer, infection, autoimmune disorder, hematopoietic disorder, wound healing disorders, inflammation.
sbg251170C EAa	An embodiment of the invention is the use of sbg251170CEAa as cell-surface molecules mediating cell-specific interactions in normal and neoplastic cells. A close homologue of sbg251170CEAa is carcinoembryonic antigen-related cell adhesion molecule 6. Carcinoembryonic antigen-related cell adhesion molecule 6 is claimed to function as a cell-surface molecules mediating cell-specific interactions in normal and neoplastic cells (1. Barnett T, Goebel SJ, Nothdurft MA, Elting JJ, Carcinoembryonic antigen family: characterization of cDNAs coding for NCA and CEA and suggestion of nonrandom sequence variation in their conserved loop-domains. Genomics 1988 Jul;3(1):59-66. 2. Inazawa J, Abe T, Inoue K, Misawa S, Oikawa S, Nakazato H, Yoshida MC. Regional assignment of nonspecific cross-reacting antigen (NCA) of the CEA gene family to chromosome 19 at band q13.2. Cytogenet Cell Genet 1989;52(1-2):28-31).	Cancer, autoimmune disorders, wound healing disorders, hematopoietic disorders and infection
sbg389686 WNT15a	An embodiment of the invention is the use of sbg389686WNT15a in regulation of cell growth and differentiation. Close homologues of sbg389686WNT15a are Wnt proteins. Wnt proteins are involved in critical developmental processes in both vertebrates and invertebrates and are implicated in regulation of cell growth and differentiation in certain adult mammalian tissues (Bergstein I, Eisenberg LM, Bhalerao J, Jenkins NA, Copeland NG, Osborne MP, Bowcock AM, Brown AM; 1997; Genomics 46:450-8). The Wnt gene family consists of at least 15 structurally related genes that encode secreted extracellular signaling factors. Wnt signaling is involved in many mammalian developmental processes, including cell proliferation, differentiation and epithelial-mesenchymal interactions, through which they contribute to the development of tissues and organs such as the limbs, the brain, the reproductive tract and the kidney. Evidence from tumor expression studies and transgenic animals experiments suggests that inappropriate activation of the Wnt signaling pathway is a major feature in human neoplasia and that oncogenic activation of this pathway can occur at many levels. Inappropriate expression of	Cancer, infection, autoimmune disorder, hematopoietic disorder, wound healing disorders, and inflammation

	the Wnt ligand and Wnt binding proteins have been found in a variety of human tumors (Smalley MJ, Dale TC;1999; Cancer Metastasis Rev 18:215-30).	
sbg236015LIPASE	An embodiment of the invention is the use of sbg236015LIPASE for treating lipase deficiency. A close homologue of sbg236015LIPASE is lysosomal acid lipase. The lysosomal acid lipase catalyzes the deacylation of triacylglyceryl and cholesteryl ester core lipids of endocytosed low density lipoproteins. This activity is deficient in patients with Wolman disease and cholesteryl ester storage disease, which are caused by a deficiency of lysosomal acid lipase activity, resulting in massive accumulation of cholesteryl ester and triglycerides (Anderson RA, Sando GN; 1991; J Biol Chem 266:22479-84).	Cancer, infection, autoimmune disorder, hematopoietic disorder, wound healing disorders, inflammation, Wolman disease, and cholesteryl ester storage disease
sbg417005LAMININ_ALPHA	An embodiment of the invention is the use of sbg417005LAMININ_ALPHA to promote myogenesis in skeletal muscle, outgrowth of neurites from central and peripheral neurons, and mesenchymal to epithelial transitions in kidney. A close homologue of sbg417005LAMININ_ALPHA is laminin. Laminins trimers, composed of alpha, beta, and gamma chains, are components of all basal laminae (BLs) throughout the bodies. In mammals they play at least three essential roles. First, they are major structural elements of BLs, forming one of two self-assembling networks to which other glycoproteins and proteoglycans of the BL attach. Second, they interact with cell surface components such as dystroglycan to attach cells to the extracellular matrix. Third, they are signaling molecules that interact with cellular receptors such as the integrins to convey important information to the cell interior. The alpha chains are ligands for most cellular laminin receptors. (Miner JH, Patton BL, Lentz SI, Gilbert DJ, Snider WD, Jenkins NA, Copeland NG, Sanes JR; 1997; J Cell Biol 137:685-701).	Cancer, infection, autoimmune disorder, hematopoietic disorder, wound healing disorders, inflammation, congenital muscular dystrophy, and junctional epidermolysis bullosa
sbg425649KINASEa	An embodiment of the invention is the use of sbg425649KINASEa in DNA replication and repair, membrane trafficking, neuroprotective, cytostatic, cardioactive, immunomodulatory, muscular, vulnerary, gastrointestinal, nephrotropic, anti-infective, gynaecological and antibacterial activities, and can be used in gene therapy. Close homologues of sbg425649KINASEa is mammalian casein kinases I (CKI) and human prostate cancer associated protein. CKI belongs to a family of serine/threonine protein kinases involved in diverse cellular processes including DNA replication and repair, membrane trafficking, circadian rhythms and Wnt signaling. Human prostate cancer associated proteins have neuroprotective, cytostatic, cardioactive, immunomodulatory, muscular, vulnerary, gastrointestinal, nephrotropic, anti-infective, gynaecological and antibacterial activities, and can be used in gene therapy.	Cancer, wound healing disorders, autoimmune disorders, hematopoietic disorders and infection

Table III (cont).

Gene Name	Uses	Associated Diseases
sbg419582P ROTOCAD HERIN	An embodiment of the invention is the use of sbg419582PROTOCADHERIN in functional systems of the nervous system, and may be involved in the formation of the neural network. A close homologue of sbg419582PROTOCADHERIN is protocadherin. The expression of protocadherin is developmentally regulated in a subset of the functional systems of the nervous system, and may be involved in the formation of the neural network by segregation of the brain nuclei and mediation of the axonal connections (Hirano S, Yan Q, Suzuki ST; 1999; J Neurosci 19:995-1005). The members of the cadherin superfamily are divided into two groups: classical cadherin type and protocadherin type. The current cadherins appear to have evolved from protocadherin (Suzuki ST; 1996; J Cell Sci 109:2609-11).	Cancer, infection, autoimmune disorder, hematopoietic disorder, wound healing disorders, inflammation, Parkinson's disease, Huntington's chorea, and multiple sclerosis
sbg453915T ECTORINa	An embodiment of the invention is the use of sbg453915TECTORINa, a secreted protein, in cellular adhesion. A close homologue of sbg453915TECTORINa is mouse tectorin beta. The beta-tectorin is a protein of 36,074 Da that contains 4 consensus N glycosylation sites and a single zona pellucida domain. It is similar to components of the sperm-egg adhesion system, and, as such may have a similar functional role (Legan PK, Rau A, Keen JN, Richardson GP, The mouse tectorins. Modular matrix proteins of the inner ear homologous to components of the sperm-egg adhesion system. J Biol Chem 1997 Mar 28;272(13):8791-801).	Infection, cancer, wound healing disorders, hemotopoietic disorders and autoimmune disorders.
SBh385630. antiinflam	An embodiment of the invention is the use of SBh385630.antiinflam in gene therapy and are also suggested to have cytokine and cell proliferation/differentiation activity, immune stimulating (e.g.vaccines) or suppressing activity, haematopoiesis regulating activity, tissue growth activity, activin/inhibin activity, chemotactic/chemokinetic activity, haemostatic and thrombolytic activity, receptor/ligand activity, anti-inflammatory activity, cadherin/tumour invasion suppressor activity, and tumour inhibition activity. Lipases are also reported to be useful for gene therapy (WO9957132-A1; Agostino, M.J., filed by GENETICS INST INC.). Close homologues of SBh385630.antiinflam include lipases.	Lematopoietic disorders, wound healing disorders, viral and bacterial infections, cancer, and autoimmune diseases
sbg471005n AChR	An embodiment of the invention is the use of sbg471005nAChR in physiological and behavioural processes of the brain. A close homologue of sbg471005nAChR is neuronal nicotinic acetylcholine receptors. Neuronal nicotinic acetylcholine receptors are a family of ion channels which are widely distributed in the human brain. There are many subtypes, and each has individual pharmacological and functional profiles. They mediate the effects of nicotine, and are involved in a number of physiological and behavioural processes. Additionally they may be implicated in a number of pathological conditions such	Cancer, infection, autoimmune disorder, hematopoietic disorder, wound healing disorders, inflammation, Alzheimer's disease, Parkinson's disease, and schizophrenia

	as Alzheimer's disease, Parkinson's disease and schizophrenia (Paterson D, Nordberg A; 2000; Prog Neurobiol 61:75-111).	
sbg442445PROa	An embodiment of the invention is the use of sbg442445PROa which may be involved in protein-protein interaction and signal transduction in immune system. sbg442445PROa was expressed predominantly in lung and spleen/lymph. It encodes a protein with leucine rich repeats which may be involved in protein-protein interaction and signal transduction in immune systems.	Inflammation, autoimmune disorders, asthma, allergies and sbg442445PROa-associated disorders
sbg456548CytoRa	The present gene has been cloned. Sybrman data showed its high expression levels in placenta and moderate levels in spleen and lymph. A close homologue of sbg456548CytoRa is another Class II cytokine receptor, ZCYTOR7. An embodiment of the invention is the use of sbg456548CytoRa, a decoy receptor, in the identification of other ligands, the promotion of anti-microbial activation of these cells, and/or potentiate the effectiveness of the natural ligand. Growth factors are known to promote the progression of cancer. A decoy receptor could interfere with that process. Proliferation, survival and differentiation can be transduced from activated cytokine receptors (Cell Signal. 1998. 10(9):619-628). Blocking these events could be crucial in modulating various diseases. The decoy receptor could potentially interfere with binding of these or other putative ligands, preventing downstream effects (Blood. 1999. 94(6):1943-1951). GM-CSF also has anti-apoptotic activity. A decoy receptor might then be able to block GM-CSF's anti-apoptotic actions when appropriate (Mol Biol Cell. 1999. 10(11):3959-3970). Roles for blocking the activity of the decoy receptor can be envisioned. GM-CSF promotes anti-microbial functions of mature neutrophils. Inhibiting the activity of an interfering decoy receptor could promote anti-microbial activation of these cells. Furthermore, rhGM-CSF is in wide clinical use to fight acute myeloid leukemia (Haematologica. 1991. 82(2): 239-245). Inhibition of a decoy receptor could potentiate the effectiveness of the natural ligand.	Chronic and acute inflammation, allergy, arthritis (including rheumatoid arthritis), septicemia, autoimmune diseases (e.g., inflammatory bowel disease, psoriasis), transplant rejection, graft vs. host disease, infection, stroke, ischemia, acute respiratory disease syndrome, asthma, restenosis, brain injury, AIDS, bone diseases, cancer, atherosclerosis, Alzheimers disease, , hematopoietic disorder, and wound healing disorder
sbg442358PROa	An embodiment of the invention is the use of sbg442358PROa useful in the prevention and treatment of cancers, cell proliferation, cardiovascular, reproductive, immune, musculoskeletal, developmental and gastrointestinal disorders and inflammation. Close homologues of sbg442358PROa are human protein B27231 and Drosophila LRR47 that also contains leucine-rich repeats (LRRs) motifs. LRR has been found in a variety of extracellular, membrane and cytoplasmic proteins and are believed to mediate specific protein-protein interactions and to function in cellular adhesion (Ntwasa, M., Buchanan, S.G. and Gay, N.J. Biochim. Biophys. Acta 1218 (2), 181-186 (1994)).	Cancer, autoimmune disorders, hemotopoietic disorders, wound healing disorders and infections

**Table IV. Quantitative, Tissue-specific mRNA expression detected using SybrMan**

Quantitative, tissue-specific, mRNA expression patterns of the genes were measured using SYBR-Green Quantitative PCR (Applied Biosystems, Foster City, CA; see Schmittgen T.D. et al., Analytical Biochemistry 285:194-204, 2000) and human cDNAs prepared from various human tissues. Gene-specific PCR primers were designed using the first nucleic acid sequence listed in the Sequence List for each gene. Results are presented as the number of copies of each specific gene's mRNA detected in 1ng mRNA pool from each tissue. Two replicate mRNA measurements were made from each tissue RNA.

Gene Name sbg237163LIPASE

Gene Name	Tissue-Specific mRNA Expression (copies per ng mRNA; avg. $\pm$ range for 2 data points per tissue)						
	Brain	Heart	Lung	Liver	Kidney	Skeletal muscle	Intestine
sbg237163LIPASE	5 $\pm 0$	8 $\pm 2$	7 $\pm 2$	-6 $\pm 1$	5 $\pm 1$	5 $\pm 2$	4 $\pm 6$

10 Gene Name sbg237163LIPASE cont.

Gene Name	Tissue-Specific mRNA Expression (copies per ng mRNA; avg. $\pm$ range for 2 data points per tissue)			
	Spleen/lymph	Placenta	Testis	
sbg237163LIPASE	3 $\pm 2$	1 $\pm 1$	47 $\pm 1$	

Gene Name sbg251170CEAa

Gene Name	Tissue-Specific mRNA Expression (copies per ng mRNA; avg. $\pm$ range for 2 data points per tissue)						
	Brain	Heart	Lung	Liver	Kidney	Skeletal muscle	Intestine
sbg251170CEAa	3 $\pm 1$	19 $\pm 1$	30 $\pm 5$	-5 $\pm 3$	3 $\pm 1$	5 $\pm 5$	21 $\pm 2$

15 Gene Name sbg251170CEAa cont.

Gene Name	Tissue-Specific mRNA Expression (copies per ng mRNA; avg. $\pm$ range for 2 data points per tissue)			
	Spleen/lymph	Placenta	Testis	
sbg237163LIPASE	33 $\pm 4$	22 $\pm 3$	14 $\pm 0$	

**Table IV (cont).**

20 In each gene's first subset table, two replicate measurements of gene of identification (GOI) mRNA were measured from various human tissues (column 2 and 3). The average GOI mRNA copies of the two replicates were made from each tissue RNA (column 4). The average amount of 18S rRNA from each tissue RNA was measured (column 5) and used for normalization. To make each tissue with the same amount of 50 ng of 18S rRNA, the normalization factor (column 6) was calculated by dividing 50 ng with



the amount of 18S rRNA measured from each tissue (column 5). The mRNA copies per 50 ng of total RNA were obtained by multiplying each GOI normalization factor and average mRNA copies (column7).

Fold changes shown in each gene's second subset table were only calculated for disease tissues which have a normal counterpart. There are blanks in the fold change column for all samples that do not have counterparts. In addition, the fold change calculations are the fold change in the disease sample as compared to the normal sample. Accordingly, there will not be a fold change calculation next to any of the normal samples. For patient matched cancer pairs (colon, lung, and breast), each tumor is compared to its specific normal counterpart. When patient-matched normal/disease pairs do not exist, each disease sample was compared back to the average of all the normal samples of that same tissue type. For example, normal brain from the same patient that provided Alzheimer's brain is not applicable. Three normal brain samples and 4 Alzheimer's brain samples are used in the fold change. Three normal samples were averaged, and each of the Alzheimer's samples was compared back to that average.

### Abbreviations

ALZ Alzheimer's Disease  
 CT CLONTECH (1020 East Meadow Circle Palo Alto, CA 94303-4230, USA)  
 KC Sample prepared by GSK investigator  
 COPD chronic obstructive pulmonary disease  
 endo endothelial  
 VEGF vascular endothelial growth factor  
 bFGF basic fibroblast growth factor  
 BM bone marrow  
 osteo osteoblast  
 OA osteoarthritis  
 RA rheumatoid arthritis  
 PBL peripheral blood lymphocytes  
 PBMNC peripheral blood mononuclear cells  
 HIV human immunodeficiency virus  
 HSV Herpes simplex virus  
 HPV human papilloma virus

### Gene Name sbg389686WNT15a

Strong expression in Brain and dendritic cells. Brain expression may be from presence of glial cells. Expression in RA and OA synovium along with dendritic cells suggests a role for this protein in these diseases. Down regulation in ischemic and dilated heart indicates that replacement of protein could be therapeutic.

Sample sbg389686WNT15a	Mean GOI copies (sample 1)	Mean GOI copies (sample 2)	Average GOI Copies	18S rRNA (ng)	50 ng/18S rRNA (ng)	copies of mRNA detected/ 50 ng total RNA
Subcutaneous Adipocytes Zenbio	0.00	0.00	0.00	3.06	16.34	0.00
Subcutaneous Adipose Zenbio	0.00	1.71	0.86	0.96	52.36	44.76
Adrenal Gland Clontech	2.29	4.18	3.24	0.61	81.97	265.16
Whole Brain Clontech	698.52	625.01	661.77	7.24	6.91	4570.20
Fetal Brain Clontech	4.14	6.78	5.46	0.48	103.95	567.57
Cerebellum Clontech	2.02	3.63	2.83	2.17	23.04	65.09
Cervix	3.16	10.14	6.65	2.42	20.66	137.40

Colon	2.48	3.44	2.96	2.71	18.45	54.61
Endometrium	2.69	5.20	3.95	0.73	68.21	269.10
Esophagus	10.67	3.24	6.96	1.37	36.50	253.83
Heart Clontech	9.26	6.07	7.67	1.32	37.88	290.34
Hypothalamus	7.10	5.16	6.13	0.32	155.28	951.86
Ileum	2.04	10.37	6.21	2.58	19.38	120.25
Jejunum	36.78	27.16	31.97	6.60	7.58	242.20
Kidney	16.46	16.55	16.51	2.12	23.58	389.27
Liver	14.07	3.34	8.71	1.50	33.33	290.17
Fetal Liver Clontech	4.60	8.89	6.75	10.40	4.81	32.43
Lung	3.11	10.49	6.80	2.57	19.46	132.30
Mammary Gland Clontech	3.28	10.61	6.95	13.00	3.85	26.71
Myometrium	1.79	13.84	7.82	2.34	21.37	166.99
Omentum	1.96	2.65	2.31	3.94	12.69	29.25
Ovary	4.50	1.71	3.11	4.34	11.52	35.77
Pancreas	3.40	2.41	2.91	0.81	61.80	179.54
Head of Pancreas	2.22	4.63	3.43	1.57	31.85	109.08
Parotid Gland	5.48	2.07	3.78	5.48	9.12	34.44
Placenta Clontech	15.15	12.80	13.98	5.26	9.51	132.84
Prostate	3.39	7.44	5.42	3.00	16.67	90.25
Rectum	2.98	3.94	3.46	1.23	40.65	140.65
Salivary Gland Clontech	3.24	1.61	2.43	7.31	6.84	16.59
Skeletal Muscle Clontech	2.01	1.55	1.78	1.26	39.68	70.63
Skin	2.69	3.45	3.07	1.21	41.32	126.86
Small Intestine Clontech	5.39	1.67	3.53	0.98	51.07	180.29
Spleen	3.96	2.52	3.24	4.92	10.16	32.93
Stomach	1.08	5.33	3.21	2.73	18.32	58.70
Testis Clontech	3.27	2.88	3.08	0.57	87.87	270.21
Thymus Clontech	5.43	4.42	4.93	9.89	5.06	24.90
Thyroid	2.32	3.01	2.67	2.77	18.05	48.10
Trachea Clontech	1.64	4.25	2.95	9.71	5.15	15.16
Urinary Bladder	3.63	6.81	5.22	5.47	9.14	47.71
Uterus	31.55	11.10	21.33	5.34	9.36	199.67

Sample sbg389686WNT15a	Reg number	Mean GOI	copies of mRNA	Sample	Fold Change in Disease
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	(GSK identifier)	copies	detected/50 ng total RNA		Population
colon normal GW98-167	21941	36.16	72.32	colon normal	
colon tumor GW98-166	21940	71.5	143.00	colon tumor	1.977323009
colon normal GW98-178	22080	2.09	4.18	colon normal	
colon tumor GW98-177	22060	9.84	19.68	colon tumor	4.708133971
colon normal GW98-561	23514	13.09	26.18	colon normal	
colon tumor GW98-560	23513	15.11	30.22	colon tumor	1.154316272
colon normal GW98-894	24691	8.62	17.24	colon normal	
colon tumor GW98-893	24690	5.76	11.52	colon tumor	-1.496527778
lung normal GW98-3	20742	140.19	280.38	lung normal	
lung tumor GW98-2	20741	1.67	3.34	lung tumor	-83.94610778
lung normal GW97-179	20677	60.54	121.08	lung normal	
lung tumor GW97-178	20676	135.62	271.24	lung tumor	2.240171787
lung normal GW98-165	21922	257.96	515.92	lung normal	
lung tumor GW98-164	21921	61.69	123.38	lung tumor	-4.181552926
lung normal GW98-282	22584	49.3	98.60	lung normal	
lung tumor GW98-281	22583	12.39	24.78	lung tumor	-3.979015335
breast normal GW00-392	28750	71.94	71.94	breast normal	
breast tumor GW00-391	28746	41.4	82.80	breast tumor	1.150959133
breast normal GW00-413	28798	19.37	19.37	breast normal	
breast tumor GW00-412	28797	1.13	2.26	breast tumor	-8.57079646
breast normal GW00-235:238	27592-95	8.19	8.19	breast normal	
breast tumor GW00-231:234	27588-91	38.27	38.27	breast tumor	4.672771673
breast normal GW98-621	23656	77.26	154.52	breast normal	
breast tumor GW98-620	23655	37.57	75.14	breast tumor	-2.056428001
brain normal BB99-542	25507	597.17	1194.34	brain normal	
brain normal BB99-406	25509	104.34	208.68	brain normal	
brain normal BB99-904	25546	282.15	564.30	brain normal	
brain stage 5 ALZ BB99-874	25502	84.26	168.52	brain stage 5 ALZ	-3.891367988
brain stage 5 ALZ BB99-887	25503	247.01	494.02	brain stage 5 ALZ	-1.327422641
brain stage 5 ALZ BB99-862	25504	173.02	346.04	brain stage 5 ALZ	-1.895079567
brain stage 5 ALZ BB99-927	25542	253.73	507.46	brain stage 5 ALZ	-1.292266057
CT lung KC	normal	146.22	292.44	CT lung	
lung 26 KC	normal	150.46	150.46	lung 26	
lung 27 KC	normal	0	0.00	lung 27	
lung 24 KC	COPD	4.76	4.76	lung 24	-23.36292017
lung 28 KC	COPD	10.06	10.06	lung 28	-11.05442346
lung 23 KC	COPD	2.75	2.75	lung 23	-40.43909091
lung 25 KC	COPD	1.93	1.93	lung 25	
asthmatic lung	29321	20.88	20.88	asthmatic	-5.326029693

ODO3112				lung	
asthmatic lung ODO3433	29323	133.29	266.58	asthmatic lung	2.397140481
asthmatic lung ODO3397	29322	322.77	645.54	asthmatic lung	5.804824315
asthmatic lung ODO4928	29325	43.52	87.04	asthmatic lung	-1.277659697
endo cells KC	control	1.89	1.89	endo cells	
endo VEGF KC		0	0.00	endo VEGF	-1.89
endo bFGF KC		1.17	1.17	endo bFGF	-1.615384615
heart Clontech	normal	153.9	307.80	heart	
heart ( T-1 ) ischemic	29417	137.74	275.48	heart T-1	-1.117322492
heart (T-14) non- obstructive DCM	29422	87.79	175.58	heart T-14	-1.753047044
heart (T-3399) DCM	29426	43.68	87.36	heart T-3399	-3.523351648
adenoid GW99-269	26162	17.62	35.24	adenoid	
tonsil GW98-280	22582	52.34	104.68	tonsil	
T cells PC00314	28453	8.45	16.90	T cells	
PBMNC KC		1.99	1.99	PBMNC	
monocyte KC		4.74	9.48	monocyte	
B cells PC00665	28455	7.65	15.30	B cells	
dendritic cells 28441		194.97	389.94	dendritic cells	
neutrophils	28440	2.13	2.13	neutrophils	
eosinophils	28446	7.25	14.50	eosinophils	
BM unstim KC		0	0.00	BM unstim	
BM stim KC		0	0.00	BM stim	0
osteo dif KC		1.48	1.48	osteo dif	
osteo undif KC		7.41	7.41	osteo undif	5.006756757
chondrocytes		26.64	66.60	chondrocyte s	
OA Synovium IP12/01	29462	476.3	476.30	OA Synovium	
OA Synovium NP10/01	29461	151.36	302.72	OA Synovium	
OA Synovium NP57/00	28464	165.01	330.02	OA Synovium	
RA Synovium NP03/01	28466	84.02	168.04	RA Synovium	
RA Synovium NP71/00	28467	184.75	369.50	RA Synovium	
RA Synovium NP45/00	28475	223.3	446.60	RA Synovium	
OA bone (biobank)	29217	72.31	72.31	OA bone (biobank)	
OA bone Sample 1	J. Emory	10.46	20.92	OA bone	
OA bone Sample 2	J. Emory	111.79	223.58	OA bone	
Cartilage (pool)	Normal	215.54	431.08	Cartilage (pool)	
Cartilage (pool)	OA	81.85	163.70	Cartilage (pool)	-2.633353696
PBL uninfected	28441	2.31	4.62	PBL uninfected	

PBL HIV IIIB	28442	2.28	4.56	PBL HIV IIIB	-1.013157895
MRC5 uninfected (100%)	29158	2.37	4.74	MRC5 uninfected (100%)	
MRC5 HSV strain F	29178	37.5	75.00	MRC5 HSV strain F	15.82278481
W12 cells	29179	0.93	1.86	W12 cells	
Keratinocytes	29180	1.33	2.66	Keratinocytes	

**Gene Name sbg389686WNT15a**

Disease tissues	Fold Change in Disease Population Relative to Normal
colon tumor	1.98
colon tumor	4.71
colon tumor	1.15
colon tumor	-1.50
lung tumor	-83.95
lung tumor	2.24
lung tumor	-4.18
lung tumor	-3.98
breast tumor	1.15
breast tumor	-8.57
breast tumor	4.67
breast tumor	-2.06
brain stage 5 ALZ	-3.89
brain stage 5 ALZ	-1.33
brain stage 5 ALZ	-1.90
brain stage 5 ALZ	-1.29
lung 24	-23.36
lung 28	-11.05
lung 23	-40.44
asthmatic lung	-5.33
asthmatic lung	2.40
asthmatic lung	5.80
asthmatic lung	-1.28
endo VEGF	-1.89
endo bFGF	-1.62
heart T-1	-1.12
heart T-14	-1.75
heart T-3399	-3.52
BM stim	0.00
osteo undif	5.01
Cartilage (pool)	-2.63
PBL HIV IIIB	-1.01
MRC5 HSV strain F	15.82

5

**Gene Name sbg236015LIPASE**

Strongly expressed in neutrophils and eosinophils suggesting an immune system function.

Additional expression is seen in RA and OA synovium and 1/3 OA bone samples. This suggests an involvement of 236015 in RA and OA. The high expression in skin when taken together with expression in neutrophils and eosinophils suggests possible involvement in immune pathologies of the skin ie.

Eosinophilia, psoriasis and eczema. The expression in eosinophils also suggests involvement in allergic reactions. Expression in neutrophils suggests role in anti-infectives.

5

Sample sbg236015LIPASE	Mean GOI copies (sample 1)	Mean GOI copies (sample 2)	Average GOI Copies	18S rRNA (ng)	50 ng/18S rRNA (ng)	copies of mRNA detected/ 50 ng total RNA
Subcutaneous Adipocytes Zenbio	0.00	11.45	5.73	3.06	16.34	93.55
Subcutaneous Adipose Zenbio	0.00	1.33	0.67	0.96	52.36	34.82
Adrenal Gland Clontech	0.52	5.04	2.78	0.61	81.97	227.87
Whole Brain Clontech	15.73	14.55	15.14	7.24	6.91	104.56
Fetal Brain Clontech	1.02	0.94	0.98	0.48	103.95	101.87
Cerebellum Clontech	0.38	0.39	0.39	2.17	23.04	8.87
Cervix	16.33	20.03	18.18	2.42	20.66	375.62
Colon	32.41	50.89	41.65	2.71	18.45	768.45
Endometrium	0.40	0.42	0.41	0.73	68.21	27.97
Esophagus	5.45	22.47	13.96	1.37	36.50	509.49
Heart Clontech	0.92	0.00	0.46	1.32	37.88	17.42
Hypothalamus	0.50	1.59	1.05	0.32	155.28	162.27
Ileum	41.95	1.51	21.73	2.58	19.38	421.12
Jejunum	7.59	15.40	11.50	6.60	7.58	87.08
Kidney	5.32	6.82	6.07	2.12	23.58	143.16
Liver	12.64	19.46	16.05	1.50	33.33	535.00
Fetal Liver Clontech	10.02	5.90	7.96	10.40	4.81	38.27
Lung	22.86	24.78	23.82	2.57	19.46	463.42
Mammary Gland Clontech	1.53	20.56	11.05	13.00	3.85	42.48
Myometrium	16.05	1.34	8.70	2.34	21.37	185.79
Omentum	8.33	9.88	9.11	3.94	12.69	115.55
Ovary	8.22	14.40	11.31	4.34	11.52	130.30
Pancreas	0.00	1.58	0.79	0.81	61.80	48.83
Head of Pancreas	0.00	1.98	0.99	1.57	31.85	31.53
Parotid Gland	5.30	11.45	8.38	5.48	9.12	76.41
Placenta Clontech	11.93	1.22	6.58	5.26	9.51	62.50
Prostate	0.00	0.00	0.00	3.00	16.67	0.00
Rectum	6.96	1.27	4.12	1.23	40.65	167.28
Salivary Gland Clontech	0.34	0.53	0.44	7.31	6.84	2.98
Skeletal Muscle Clontech	176.88	0.41	88.65	1.26	39.68	3517.66
Skin	95.17	147.16	121.17	1.21	41.32	5006.82
Small Intestine	0.35	1.31	0.83	0.98	51.07	42.39

Clontech						
Spleen	105.73	80.76	93.25	4.92	10.16	947.61
Stomach	0.56	3.73	2.15	2.73	18.32	39.29
Testis Clontech	0.79	0.78	0.79	0.57	87.87	68.98
Thymus Clontech	22.00	22.48	22.24	9.89	5.06	112.44
Thyroid	0.65	0.48	0.57	2.77	18.05	10.20
Trachea Clontech	1.20	0.00	0.60	9.71	5.15	3.09
Urinary Bladder	5.59	8.67	7.13	5.47	9.14	65.17
Uterus	19.26	27.10	23.18	5.34	9.36	217.04

Sample sbg236015LIPASE	Reg number (GSK identifier)	Mean GOI copies	copies of mRNA detected/50 ng total RNA	Sample	Fold Change in Disease Population
colon normal GW98-167	21941	58.7	117.40	colon normal	
colon tumor GW98-166	21940	300.92	601.84	colon tumor	5.126405451
colon normal GW98-178	22080	8.78	17.56	colon normal	
colon tumor GW98-177	22060	23.74	47.48	colon tumor	2.703872437
colon normal GW98-561	23514	27.1	54.20	colon normal	
colon tumor GW98-560	23513	39.16	78.32	colon tumor	1.44501845
colon normal GW98-894	24691	10.15	20.30	colon normal	
colon tumor GW98-893	24690	144.58	289.16	colon tumor	14.24433498
lung normal GW98-3	20742	165.8	331.60	lung normal	
lung tumor GW98-2	20741	80.9	161.80	lung tumor	-2.049443758
lung normal GW97-179	20677	37.81	75.62	lung normal	
lung tumor GW97-178	20676	109.72	219.44	lung tumor	2.90187781
lung normal GW98-165	21922	150.06	300.12	lung normal	
lung tumor GW98-164	21921	169.73	339.46	lung tumor	1.131080901
lung normal GW98-282	22584	489.42	978.84	lung normal	
lung tumor GW98-281	22583	188.22	376.44	lung tumor	-2.600255021
breast normal GW00-392	28750	44.86	44.86	breast normal	
breast tumor GW00-391	28746	46.35	92.70	breast tumor	2.06642889
breast normal GW00-413	28798	16.35	16.35	breast normal	
breast tumor GW00-412	28797	55.98	111.96	breast tumor	6.847706422
breast normal GW00-235:238	27592-95	3.84	3.84	breast normal	
breast tumor GW00-231:234	27588-91	35.8	35.80	breast tumor	9.322916667
breast normal GW98-621	23656	12.14	24.28	breast normal	
breast tumor GW98-620	23655	44.85	89.70	breast tumor	3.694398682
brain normal BB99-542	25507	26.03	52.06	brain normal	
brain normal BB99-406	25509	14.78	29.56	brain normal	
brain normal BB99-904	25546	3.39	6.78	brain normal	
brain stage 5 ALZ BB99-874	25502	35.71	71.42	brain stage 5 ALZ	2.423755656
brain stage 5 ALZ BB99-887	25503	9.11	18.22	brain stage 5 ALZ	-1.617270399

brain stage 5 ALZ BB99-862	25504	8.18	16.36	brain stage 5 ALZ	-1.801140994
brain stage 5 ALZ BB99-927	25542	46.37	92.74	brain stage 5 ALZ	3.147285068
CT lung KC	normal	80.77	161.54	CT lung	
lung 26 KC	normal	233.65	233.65	lung 26	
lung 27 KC	normal	75.27	75.27	lung 27	
lung 24 KC	COPD	68.64	68.64	lung 24	-1.876821096
lung 28 KC	COPD	94.1	94.10	lung 28	-1.369022317
lung 23 KC	COPD	88.48	88.48	lung 23	-1.455978752
lung 25 KC	normal	44.84	44.84	lung 25	
asthmatic lung ODO3112	29321	111.42	111.42	asthmatic lung	-1.156210734
asthmatic lung ODO3433	29323	566.5	1133.00	asthmatic lung	8.794876771
asthmatic lung ODO3397	29322	262.77	525.54	asthmatic lung	4.079487677
asthmatic lung ODO4928	29325	367.52	735.04	asthmatic lung	5.70572482
endo cells KC	control	3.23	3.23	endo cells	
endo VEGF KC		3.41	3.41	endo VEGF	1.055727554
endo bFGF KC		0	0.00	endo bFGF	-3.23
heart Clontech	normal	0	0.00	heart	
heart ( T-1 ) ischemic	29417	35.96	71.92	heart T-1	71.92
heart (T-14) non-obstructive DCM	29422	18.72	37.44	heart T-14	37.44
heart (T-3399) DCM	29426	37.97	75.94	heart T-3399	75.94
adenoid GW99-269	26162	14.17	28.34	adenoid	
tonsil GW98-280	22582	51.21	102.42	tonsil	
T cells PC00314	28453	111.1	222.20	T cells	
PBMNC KC		162.01	162.01	PBMNC	
monocyte KC		90.49	180.98	monocyte	
B cells PC00665	28455	109.71	219.42	B cells	
dendritic cells 28441		2.44	4.88	dendritic cells	
neutrophils	28440	1110.91	1110.91	neutrophils	
eosinophils	28446	835.72	1671.44	eosinophils	
BM unstim KC		181.05	181.05	BM unstim	
BM stim KC		93.96	93.96	BM stim	-1.92688378
osteo dif KC		0	0.00	osteo dif	
osteo undif KC		0.72	0.72	osteo undif	0.72
chondrocytes		2.03	5.08	chondrocytes	
OA Synovium IP12/01	29462	27.82	27.82	OA Synovium	
OA Synovium NP10/01	29461	84.94	169.88	OA Synovium	
OA Synovium NP57/00	28464	46.58	93.16	OA Synovium	
RA Synovium NP03/01	28466	248.24	496.48	RA Synovium	
RA Synovium NP71/00	28467	148.32	296.64	RA Synovium	



RA Synovium NP45/00	28475	260.28	520.56	RA Synovium	
OA bone (biobank)	29217	10.27	10.27	OA bone (biobank)	
OA bone Sample 1	J. Emory	17.32	34.64	OA bone	
OA bone Sample 2	J. Emory	657.01	1314.02	OA bone	
Cartilage (pool)	Normal	59.17	118.34	Cartilage (pool)	
Cartilage (pool)	OA	23.33	46.66	Cartilage (pool)	-2.53621946
PBL uninfected	28441	23.51	47.02	PBL uninfected	
PBL HIV IIIB	28442	5.86	11.72	PBL HIV IIIB	-4.011945392
MRC5 uninfected (100%)	29158	3.79	7.58	MRC5 uninfected (100%)	
MRC5 HSV strain F	29178	80.19	160.38	MRC5 HSV strain F	21.15831135
W12 cells	29179	95.42	190.84	W12 cells	
Keratinocytes	29180	16.18	32.36	Keratinocytes	

Gene Name sbg236015LIPASE

Disease tissues	Fold Change in Disease Population Relative to Normal
colon tumor	5.13
colon tumor	2.70
colon tumor	1.45
colon tumor	14.24
lung tumor	-2.05
lung tumor	2.90
lung tumor	1.13
lung tumor	-2.60
breast tumor	2.07
breast tumor	6.85
breast tumor	9.32
breast tumor	3.69
brain stage 5 ALZ	2.42
brain stage 5 ALZ	-1.62
brain stage 5 ALZ	-1.80
brain stage 5 ALZ	3.15
lung 24	-1.88
lung 28	-1.37
lung 23	-1.46
asthmatic lung	-1.16
asthmatic lung	8.79
asthmatic lung	4.08
asthmatic lung	5.71
endo VEGF	1.06
endo bFGF	-3.23
heart T-1	71.92

heart T-14	37.44
heart T-3399	75.94
BM stim	-1.93
osteo undif	0.72
Cartilage (pool)	-2.54
PBL HIV IIIB	-4.01
MRC5 HSV strain F	21.16

**Gene Name sbg417005LAMININ**

Expression in adenoid, tonsil and B-cells with corroborating expression in RA/OA samples and asthmatic lung (1/4) suggests involvement in these diseases. Strong expression in brain with overexpression in Alzheimer's disease indicates a role in AD. Down regulation in HSV infected cells suggests potential host cell factor. Expression in colon and lung normal/tumor pairs without corroborating expression in normal tissues suggests immune cell infiltrates.

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Sample sbg417005LAMININ	Mean GOI copies (sample 1)	Mean GOI copies (sample 2)	Average GOI Copies	18S rRNA (ng)	50 ng/18S rRNA (ng)	copies of mRNA detecte d/50 ng total RNA
Subcutaneous Adipocytes Zenbio	60.2785303	73.59679955	66.94	3.06	16.34	1093.75
Subcutaneous Adipose Zenbio	3.032572965	1.985862153	2.51	0.96	52.36	131.37
Adrenal Gland Clontech	0.965703497	0.965703497	0.97	0.61	81.97	79.16
Whole Brain Clontech	4131.557992	6997.879078	5564.72	7.24	6.91	38430.38
Fetal Brain Clontech	0.965703497	3.268211325	2.12	0.48	103.95	220.06
Cerebellum Clontech	3.301057867	17.3966665	10.35	2.17	23.04	238.45
Cervix	5.920484049	7.517891571	6.72	2.42	20.66	138.83
Colon	35.48962684	22.53180605	29.01	2.71	18.45	535.25
Endometrium	11.59757492	0.965703497	6.28	0.73	68.21	428.49
Esophagus	7.098528857	3.523216475	5.31	1.37	36.50	193.83
Heart Clontech	0.965703497	5.368977287	3.17	1.32	37.88	119.98
Hypothalamus	0.965703497	0.965703497	0.97	0.32	155.28	149.95
Ileum	30.81006847	14.15032296	22.48	2.58	19.38	435.66
Jejunum	44.08994058	30.29386314	37.19	6.60	7.58	281.76
Kidney	9.424973981	15.68529125	12.56	2.12	23.58	296.11
Liver	3.742288161	0.965703497	2.35	1.50	33.33	78.47
Fetal Liver Clontech	94.45949484	93.8962252	94.18	10.40	4.81	452.78
Lung	13.84782444	19.95367566	16.90	2.57	19.46	328.81
Mammary Gland Clontech	107.7956161	95.02632495	101.41	13.00	3.85	390.04
Myometrium	12.50117866	14.93742804	13.72	2.34	21.37	293.15
Omentum	13.998213	22.03816357	18.02	3.94	12.69	228.66
Ovary	0.965703497	0.965703497	0.97	4.34	11.52	11.13
Pancreas	2.254750425	0.965703497	1.61	0.81	61.80	99.52
Head of Pancreas	0.965703497	0.965703497	0.97	1.57	31.85	30.75
Parotid Gland	25.8930892	14.85668173	20.37	5.48	9.12	185.90

Placenta Clontech	83.84029668	95.02632495	89.43	5.26	9.51	850.13
Prostate	8.047386733	15.18245262	11.61	3.00	16.67	193.58
Rectum	10.53572882	20.06385011	15.30	1.23	40.65	621.94
Salivary Gland Clontech	62.43024331	57.19623352	59.81	7.31	6.84	409.12
Skeletal Muscle Clontech	1.376746214	0.965703497	1.17	1.26	39.68	46.48
Skin	0.965703497	0.965703497	0.97	1.21	41.32	39.91
Small Intestine Clontech	0.965703497	0.965703497	0.97	0.98	51.07	49.32
Spleen	0.965703497	5.740147492	3.35	4.92	10.16	34.07
Stomach	0.965703497	0.965703497	0.97	2.73	18.32	17.69
Testis Clontech	0.965703497	0.965703497	0.97	0.57	87.87	84.86
Thymus Clontech	258.7386545	207.7169358	233.23	9.89	5.06	1179.11
Thyroid	12.56849785	19.09489343	15.83	2.77	18.05	285.77
Trachea Clontech	24.35330878	31.87047641	28.11	9.71	5.15	144.76
Urinary Bladder	51.81831091	57.53035871	54.67	5.47	9.14	499.77
Uterus	13.12099559	14.61718971	13.87	5.34	9.36	129.86

Sample sbg417005LAMININ	Reg. number (GSK identifier )	Mean GOI copies	copies of mRNA detected/50 ng total RNA	Sample	Fold Change in Disease Population
colon normal GW98-167	21941	15446.92728	30893.85	colon normal	
colon tumor GW98-166	21940	23910.90415	47821.81	colon tumor	1.547939193
colon normal GW98-178	22080	14621.97321	29243.95	colon normal	
colon tumor GW98-177	22060	2058.30396	4116.61	colon tumor	-7.10389403
colon normal GW98-561	23514	5590.900474	11181.80	colon normal	
colon tumor GW98-560	23513	12318.10362	24636.21	colon tumor	2.203241442
colon normal GW98-894	24691	4478.692403	8957.38	colon normal	
colon tumor GW98-893	24690	7546.100944	15092.20	colon tumor	1.684889308
lung normal GW98-3	20742	23910.90415	47821.81	lung normal	
lung tumor GW98-2	20741	35021.23317	70042.47	lung tumor	1.464655328
lung normal GW97-179	20677	23341.61421	46683.23	lung normal	
lung tumor GW97-178	20676	24103.90252	48207.81	lung tumor	1.032657909
lung normal GW98-165	21922	18374.41273	36748.83	lung normal	
lung tumor GW98-164	21921	34735.19726	69470.39	lung tumor	1.890411289
lung normal GW98-282	22584	3002.298467	6004.60	lung normal	
lung tumor GW98-281	22583	3519.560955	7039.12	lung tumor	1.172288829
breast normal GW00-392	28750	5978.671937	5978.67	breast normal	
breast tumor GW00-391	28746	5674.721186	11349.44	breast tumor	1.898321649
breast normal GW00-413	28798	1523.643258	1523.64	breast normal	
breast tumor GW00-412	28797	956.0902914	1912.18	breast tumor	1.255005444
breast normal GW00-235:238	27592-95	760.6128764	760.61	breast normal	
breast tumor GW00-	27588-91	4192.50003	4192.50	breast tumor	5.51200244

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breast normal GW98-621	23656	5674.721186	11349.44	breast normal	
breast tumor GW98-620	23655	8017.202071	16034.40	breast tumor	1.412792243
brain normal BB99-542	25507	791.7818289	1583.56	brain normal	
brain normal BB99-406	25509	524.990001	1049.98	brain normal	
brain normal BB99-904	25546	396.8655236	793.73	brain normal	
brain stage 5 ALZ BB99-874	25502	3203.498645	6407.00	brain stage 5 ALZ	5.608243725
brain stage 5 ALZ BB99-887	25503	3925.505917	7851.01	brain stage 5 ALZ	6.872234505
brain stage 5 ALZ BB99-862	25504	1502.651942	3005.30	brain stage 5 ALZ	2.630635833
brain stage 5 ALZ BB99-927	25542	1555.711325	3111.42	brain stage 5 ALZ	2.723524884
CT lung KC	normal	3730.249874	7460.50	CT lung	
lung 26 KC	normal	286.3143862	286.31	lung 26	
lung 27 KC	normal	72.30560941	72.31	lung 27	
lung 24 KC	COPD	28.47771374	28.48	lung 24	-69.25877363
lung 28 KC	COPD	66.98006875	66.98	lung 28	-29.44654382
lung 23 KC	COPD	57.53035871	57.53	lung 23	-34.28331708
lung 25 KC	COPD	70.20637402	70.21	lung 25	
asthmatic lung ODO3112	29321	2304.915385	2304.92	asthmatic lung	1.168624722
asthmatic lung ODO3433	29323	3112.377018	6224.75	asthmatic lung	3.156038395
asthmatic lung ODO3397	29322	21892.2071	43784.41	asthmatic lung	22.19931768
asthmatic lung ODO4928	29325	5268.438364	10536.88	asthmatic lung	5.34234563
endo cells KC	control	396.8655236	396.87	endo cells	
endo VEGF KC		157.1987188	157.20	endo VEGF	-2.524610421
endo bFGF KC		518.1542863	518.15	endo bFGF	1.305616778
heart Clontech	normal	1865.302957	3730.61	heart	
heart ( T-1 ) ischemic	29417	3757.505456	7515.01	heart T-1	2.014421005
heart (T-14) non-obstructive DCM	29422	1633.333543	3266.67	heart T-14	-1.142022072
heart (T-3399) DCM	29426	2938.226492	5876.45	heart T-3399	1.575200683
adenoid GW99-269	26162	1238.725105	2477.45	adenoid	
tonsil GW98-280	22582	2288.625236	4577.25	tonsil	
T cells PC00314	28453	61.34444995	122.69	T cells	
PBMNC KC		5.341492957	5.34	PBMNC	
monocyte KC		3.576686692	7.15	monocyte	
B cells PC00665	28455	716.2601536	1432.52	B cells	
dendritic cells 28441		32.23243314	64.46	dendritic cells	
neutrophils	28440	32.9693996	32.97	neutrophils	
eosinophils	28446	1.444144312	2.89	eosinophils	
BM unstim KC		5.951115795	5.95	BM unstim	
BM stim KC		11.72233235	11.72	BM stim	1.969770503
osteo dif KC		10.20495465	10.20	osteo dif	

osteo undif KC		8.526098078	8.53	osteo undif	-1.196907959
chondrocytes		14621.97321	36554.93	chondrocytes	
OA Synovium IP12/01	29462	5549.480142	5549.48	OA Synovium	
OA Synovium NP10/01	29461	3545.197127	7090.39	OA Synovium	
OA Synovium NP57/00	28464	4223.325454	8446.65	OA Synovium	
RA Synovium NP03/01	28466	1221.845309	2443.69	RA Synovium	
RA Synovium NP71/00	28467	4892.67872	9785.36	RA Synovium	
RA Synovium NP45/00	28475	1080.396739	2160.79	RA Synovium	
OA bone (biobank)	29217	995.7612933	995.76	OA bone (biobank)	
OA bone Sample 1	J. Emory	982.3483914	1964.70	OA bone	
OA bone Sample 2	J. Emory	472.8535333	945.71	OA bone	
Cartilage (pool)	Normal	1213.496434	2426.99	Cartilage (pool)	
Cartilage (pool)	OA	697.4302173	1394.86	Cartilage (pool)	-1.73995391
PBL uninfected	28441	161.1142664	322.23	PBL uninfected	
PBL HIV IIIB	28442	191.5686557	383.14	PBL HIV IIIB	1.189023542
MRC5 uninfected (100%)	29158	5934.220593	11868.44	MRC5 uninfected (100%)	
MRC5 HSV strain F	29178	50.63206269	101.26	MRC5 HSV strain F	-117.2028213
W12 cells	29179	13843.2955	27686.59	W12 cells	
Keratinocytes	29180	11849.9156	23699.83	Keratinocytes	

Gene Name sbg417005LAMININ

Disease tissues	Fold Change in Disease Population Relative to Normal
colon tumor	1.55
colon tumor	-7.10
colon tumor	2.20
colon tumor	1.68
lung tumor	1.46
lung tumor	1.03
lung tumor	1.89
lung tumor	1.17
breast tumor	1.90
breast tumor	1.26
breast tumor	5.51
breast tumor	1.41
brain stage 5 ALZ	5.61
brain stage 5 ALZ	6.87

brain stage 5 ALZ	2.63
brain stage 5 ALZ	2.72
lung 24	-69.26
lung 28	-29.45
lung 23	-34.28
asthmatic lung	1.17
asthmatic lung	3.16
asthmatic lung	22.20
asthmatic lung	5.34
endo VEGF	-2.52
endo bFGF	1.31
heart T-1	2.01
heart T-14	-1.14
heart T-3399	1.58
BM stim	1.97
osteo undif	-1.20
Cartilage (pool)	-1.74
PBL HIV IIIB	1.19
MRC5 HSV strain F	-117.20

**Gene Name** sbg425649KINASEa

Strongly expressed in neutrophils and eosinophils suggesting function in immune system such as involvement in allergic reactions and anti-infective. Lower expression in T-cells. Expression in 2/3 OA bone samples indicate a role in OA. Strongly expressed in rectum and skeletal muscle, unknown function.

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Sample sbg425649KINASEa	Mean GOI copies (sample 1)	Mean GOI copies (sample 2)	Average GOI Copies	18S rRNA (ng)	50 ng/18S rRNA (ng)	copies of mRNA detected/ 50 ng total RNA
Subcutaneous Adipocytes Zenbio	0.00	0.03	0.02	3.06	16.34	0.25
Subcutaneous Adipose Zenbio	0.00	0.00	0.00	0.96	52.36	0.00
Adrenal Gland Clontech	0.23	0.00	0.12	0.61	81.97	9.43
Whole Brain Clontech	163.64	47.63	105.64	7.24	6.91	729.52
Fetal Brain Clontech	0.47	0.00	0.24	0.48	103.95	24.43
Cerebellum Clontech	0.00	0.00	0.00	2.17	23.04	0.00
Cervix	5.54	0.00	2.77	2.42	20.66	57.23
Colon	0.70	0.00	0.35	2.71	18.45	6.46
Endometrium	0.33	0.06	0.20	0.73	68.21	13.30
Esophagus	0.35	0.47	0.41	1.37	36.50	14.96
Heart Clontech	0.00	0.00	0.00	1.32	37.88	0.00
Hypothalamus	0.00	0.00	0.00	0.32	155.28	0.00
Ileum	0.00	4.49	2.25	2.58	19.38	43.51
Jejunum	0.29	0.73	0.51	6.60	7.58	3.86
Kidney	0.00	0.00	0.00	2.12	23.58	0.00
Liver	10.48	5.64	8.06	1.50	33.33	268.67
Fetal Liver Clontech	8.56	0.00	4.28	10.40	4.81	20.58
Lung	0.00	0.00	0.00	2.57	19.46	0.00
Mammary Gland Clontech	0.00	0.00	0.00	13.00	3.85	0.00

Myometrium	8.61	5.00	6.81	2.34	21.37	145.41
Omentum	0.23	10.99	5.61	3.94	12.69	71.19
Ovary	4.48	4.62	4.55	4.34	11.52	52.42
Pancreas	0.27	0.00	0.14	0.81	61.80	8.34
Head of Pancreas	0.11	0.04	0.08	1.57	31.85	2.39
Parotid Gland	0.69	4.51	2.60	5.48	9.12	23.72
Placenta Clontech	10.58	0.14	5.36	5.26	9.51	50.95
Prostate	9.74	6.18	7.96	3.00	16.67	132.67
Rectum	225.51	76.99	151.25	1.23	40.65	6148.37
Salivary Gland Clontech	60.93	67.22	64.08	7.31	6.84	438.27
Skeletal Muscle Clontech	749.28	29.78	389.53	1.26	39.68	15457.54
Skin	0.00	4.46	2.23	1.21	41.32	92.15
Small Intestine Clontech	0.73	0.00	0.37	0.98	51.07	18.64
Spleen	4.10	8.60	6.35	4.92	10.16	64.53
Stomach	4.24	19.28	11.76	2.73	18.32	215.38
Testis Clontech	10.11	6.34	8.23	0.57	87.87	722.76
Thymus Clontech	2.79	5.35	4.07	9.89	5.06	20.58
Thyroid	0.00	0.06	0.03	2.77	18.05	0.54
Trachea Clontech	5.24	14.14	9.69	9.71	5.15	49.90
Urinary Bladder	0.09	0.00	0.05	5.47	9.14	0.41
Uterus	27.26	7.61	17.44	5.34	9.36	163.25

Sample sbg425649KINASEa	Reg number (GSK identifier)	Mean GOI copies	copies of mRNA detected/50 ng total RNA	Sample	Fold Change in Disease Population
colon normal GW98-167	21941	11.11	22.22	colon normal	
colon tumor GW98-166	21940	7.3	14.60	colon tumor	-1.521917808
colon normal GW98-178	22080	0	0.00	colon normal	
colon tumor GW98-177	22060	2.57	5.14	colon tumor	5.14
colon normal GW98-561	23514	0	0.00	colon normal	
colon tumor GW98-560	23513	0	0.00	colon tumor	0
colon normal GW98-894	24691	2.71	5.42	colon normal	
colon tumor GW98-893	24690	8.51	17.02	colon tumor	3.140221402
lung normal GW98-3	20742	1.78	3.56	lung normal	
lung tumor GW98-2	20741	0	0.00	lung tumor	-3.56
lung normal GW97-179	20677	3.18	6.36	lung normal	
lung tumor GW97-178	20676	2.64	5.28	lung tumor	-1.204545455
lung normal GW98-165	21922	6.46	12.92	lung normal	
lung tumor GW98-164	21921	19.99	39.98	lung tumor	3.094427245
lung normal GW98-282	22584	31.56	63.12	lung normal	
lung tumor GW98-281	22583	7.47	14.94	lung tumor	-4.224899598
breast normal GW00-392	28750	5.68	5.68	breast normal	
breast tumor GW00-391	28746	2.87	5.74	breast tumor	1.01056338

breast normal GW00-413	28798	1.66	1.66	breast normal	
breast tumor GW00-412	28797	1.99	3.98	breast tumor	2.397590361
breast normal GW00-235:238	27592-95	0	0.00	breast normal	
breast tumor GW00-231:234	27588-91	2.19	2.19	breast tumor	2.19
breast normal GW98-621	23656	4.72	9.44	breast normal	
breast tumor GW98-620	23655	0	0.00	breast tumor	-9.44
brain normal BB99-542	25507	28.9	57.80	brain normal	
brain normal BB99-406	25509	24.84	49.68	brain normal	
brain normal BB99-904	25546	6.92	13.84	brain normal	
brain stage 5 ALZ BB99-874	25502	23.65	47.30	brain stage 5 ALZ	1.169634026
brain stage 5 ALZ BB99-887	25503	28.68	57.36	brain stage 5 ALZ	1.418397626
brain stage 5 ALZ BB99-862	25504	18.18	36.36	brain stage 5 ALZ	-1.112211221
brain stage 5 ALZ BB99-927	25542	14.18	28.36	brain stage 5 ALZ	-1.425952045
CT lung KC	normal	29.45	58.90	CT lung	
lung 26 KC	normal	2.47	2.47	lung 26	
lung 27 KC	normal	0	0.00	lung 27	
lung 24 KC	COPD	0	0.00	lung 24	-15.3425
lung 28 KC	COPD	0.3	0.30	lung 28	-51.14166667
lung 23 KC	COPD	0	0.00	lung 23	-15.3425
lung 25 KC	COPD	0	0.00	lung 25	
asthmatic lung ODO3112	29321	3.24	3.24	asthmatic lung	-4.735339506
asthmatic lung ODO3433	29323	88.32	176.64	asthmatic lung	11.51311716
asthmatic lung ODO3397	29322	55.65	111.30	asthmatic lung	7.254358807
asthmatic lung ODO4928	29325	50.64	101.28	asthmatic lung	6.601270979
endo cells KC	control	0	0.00	endo cells	
endo VEGF KC		0	0.00	endo VEGF	0
endo bFGF KC		0	0.00	endo bFGF	0
heart Clontech	normal	15.26	30.52	heart	
heart ( T-1 ) ischemic	29417	0	0.00	heart T-1	-30.52
heart (T-14) non-obstructive DCM	29422	3.69	7.38	heart T-14	-4.135501355
heart (T-3399) DCM	29426	0	0.00	heart T-3399	-30.52
adenoid GW99-269	26162	0	0.00	adenoid	
tonsil GW98-280	22582	3.65	7.30	tonsil	
T cells PC00314	28453	167.51	335.02	T cells	
PBMNC KC		2.5	2.50	PBMNC	
monocyte KC		2.37	4.74	monocyte	
B cells PC00665	28455	0	0.00	B cells	
dendritic cells 28441		0	0.00	dendritic cells	



neutrophils	28440	1576.76	1576.76	neutrophils	
eosinophils	28446	755.1	1510.20	eosinophils	
BM unstim KC		14.87	14.87	BM unstim	
BM stim KC		45.45	45.45	BM stim	3.056489576
osteo dif KC		0	0.00	osteo dif	
osteo undif KC		0	0.00	osteo undif	0
chondrocytes		7.48	18.70	chondrocytes	
OA Synovium IP12/01	29462	17.79	17.79	OA Synovium	
OA Synovium NP10/01	29461	14.09	28.18	OA Synovium	
OA Synovium NP57/00	28464	11.97	23.94	OA Synovium	
RA Synovium NP03/01	28466	6.84	13.68	RA Synovium	
RA Synovium NP71/00	28467	22.88	45.76	RA Synovium	
RA Synovium NP45/00	28475	1.64	3.28	RA Synovium	
OA bone (biobank)	29217	370.22	370.22	OA bone (biobank)	
OA bone Sample 1	J. Emory	3.21	6.42	OA bone	
OA bone Sample 2	J. Emory	311.65	623.30	OA bone	
Cartilage (pool)	Normal	32.23	64.46	Cartilage (pool)	
Cartilage (pool)	OA	2.87	5.74	Cartilage (pool)	-11.22996516
PBL uninfected	28441	4.18	8.36	PBL uninfected	
PBL HIV IIIB	28442	0	0.00	PBL HIV IIIB	-8.36
MRC5 uninfected (100%)	29158	4.4	8.80	MRC5 uninfected (100%)	
MRC5 HSV strain F	29178	11.46	22.92	MRC5 HSV strain F	2.604545455
W12 cells	29179	0	0.00	W12 cells	
Keratinocytes	29180	0	0.00	Keratinocytes	

Gene Name sbg425649KINASEa

Disease tissues	Fold Change in Disease Population Relative to Normal
colon tumor	-1.52
colon tumor	5.14
colon tumor	0.00
colon tumor	3.14
lung tumor	-3.56
lung tumor	-1.20
lung tumor	3.09
lung tumor	-4.22
breast tumor	1.01

breast tumor	2.40
breast tumor	2.19
breast tumor	-9.44
brain stage 5 ALZ	1.17
brain stage 5 ALZ	1.42
brain stage 5 ALZ	-1.11
brain stage 5 ALZ	-1.43
lung 24	-15.34
lung 28	-51.14
lung 23	-15.34
asthmatic lung	-4.74
asthmatic lung	11.51
asthmatic lung	7.25
asthmatic lung	6.60
endo VEGF	0.00
endo bFGF	0.00
heart T-1	-30.52
heart T-14	-4.14
heart T-3399	-30.52
BM stim	3.06
osteo undif	0.00
Cartilage (pool)	-11.23
PBL HIV IIIB	-8.36
MRC5 HSV strain F	2.60

**Gene Name** sbg419582PROTOCADHERIN

Brain specific expression. No correlation with Alzheimer's disease. Low expression in RA and OA synovium but no corroborating expression in immune cells. Slightly upregulated in heart disease. Overexpressed in lung (1/4) and breast (1/4) tumors.

5

Sample sbg419582PROTOCADHERIN	Mean GOI copies (sample 1)	Mean GOI copies (sample 2)	Average GOI Copies	18S rRNA (ng)	50 ng/18S rRNA (ng)	copies of mRNA detected/ 50 ng total RNA
Subcutaneous Adipocytes Zenbio	18.18	23.43	20.81	3.06	16.34	339.95
Subcutaneous Adipose Zenbio	0.11	0.33	0.22	0.96	52.36	11.52
Adrenal Gland Clontech	1.8	1.06	1.43	0.61	81.97	117.21
Whole Brain Clontech	10913.92	10314.42	10614.17	7.24	6.91	73302.28
Fetal Brain Clontech	0.31	4.68	2.50	0.48	103.95	259.36
Cerebellum Clontech	0.1	4.58	2.34	2.17	23.04	53.92
Cervix	0.22	1.22	0.72	2.42	20.66	14.88
Colon	0.31	13.73	7.02	2.71	18.45	129.52
Endometrium	0.1	0.58	0.34	0.73	68.21	23.19
Esophagus	2.21	1.96	2.09	1.37	36.50	76.09
Heart Clontech	0.32	0	0.16	1.32	37.88	6.06
Hypothalamus	0.15	1.2	0.68	0.32	155.28	104.81
Ileum	2.77	1.03	1.90	2.58	19.38	36.82
Jejunum	0.26	1.18	0.72	6.60	7.58	5.45
Kidney	1.99	0.28	1.14	2.12	23.58	26.77

Liver	7.59	12.42	10.01	1.50	33.33	333.50
Fetal Liver Clontech	18.75	11.04	14.90	10.40	4.81	71.61
Lung	7.19	0.71	3.95	2.57	19.46	76.85
Mammary Gland Clontech	88.14	97.88	93.01	13.00	3.85	357.73
Myometrium	0.51	4.8	2.66	2.34	21.37	56.73
Omentum	7.52	2.19	4.86	3.94	12.69	61.61
Ovary	13.46	4.84	9.15	4.34	11.52	105.41
Pancreas	0.49	1.02	0.76	0.81	61.80	46.66
Head of Pancreas	0.29	0.15	0.22	1.57	31.85	7.01
Parotid Gland	6.09	6.19	6.14	5.48	9.12	56.02
Placenta Clontech	10.67	2.35	6.51	5.26	9.51	61.88
Prostate	2.02	3.59	2.81	3.00	16.67	46.75
Rectum	0.54	7.25	3.90	1.23	40.65	158.33
Salivary Gland Clontech	20.51	13.73	17.12	7.31	6.84	117.10
Skeletal Muscle Clontech	1.06	0.79	0.93	1.26	39.68	36.71
Skin	13.09	0.6	6.85	1.21	41.32	282.85
Small Intestine Clontech	0.11	2.47	1.29	0.98	51.07	65.88
Spleen	1.05	11	6.03	4.92	10.16	61.23
Stomach	0.95	1.3	1.13	2.73	18.32	20.60
Testis Clontech	2.82	3.19	3.01	0.57	87.87	264.06
Thymus Clontech	117.82	118.81	118.32	9.89	5.06	598.15
Thyroid	2.34	2.29	2.32	2.77	18.05	41.79
Trachea Clontech	8.72	9.37	9.05	9.71	5.15	46.58
Urinary Bladder	14.23	16.82	15.53	5.47	9.14	141.91
Uterus	1.49	27.26	14.38	5.34	9.36	134.60

Sample sbg419582PROTOCA DHERIN	Reg number (GSK identifier)	Mean GOI copies	copies of mRNA detected/50 ng total RNA	Sample	Fold Change in Disease Population
colon normal GW98-167	21941	464.48	928.96	colon normal	
colon tumor GW98-166	21940	84.22	168.44	colon tumor	-5.515079554
colon normal GW98-178	22080	32.8	65.60	colon normal	
colon tumor GW98-177	22060	44.71	89.42	colon tumor	1.363109756
colon normal GW98-561	23514	135.5	271.00	colon normal	
colon tumor GW98-560	23513	78.51	157.02	colon tumor	-1.72589479
colon normal GW98-894	24691	454.16	908.32	colon normal	
colon tumor GW98-893	24690	51.37	102.74	colon tumor	-8.840957757
lung normal GW98-3	20742	60.35	120.70	lung normal	
lung tumor GW98-2	20741	101.98	203.96	lung tumor	1.689809445
lung normal GW97-179	20677	264	528.00	lung normal	
lung tumor GW97-178	20676	78.49	156.98	lung tumor	-3.363485794
lung normal GW98-165	21922	88.19	176.38	lung normal	
lung tumor GW98-164	21921	7554.58	15109.16	lung tumor	85.66254677

lung normal GW98-282	22584	344.2	688.40	lung normal	
lung tumor GW98-281	22583	45.51	91.02	lung tumor	-7.563172929
breast normal GW00-392	28750	132.43	132.43	breast normal	
breast tumor GW00-391	28746	98.14	196.28	breast tumor	1.482141509
breast normal GW00-413	28798	154.37	154.37	breast normal	
breast tumor GW00-412	28797	1289.09	2578.18	breast tumor	16.70130207
breast normal GW00-235:238	27592-95	18.63	18.63	breast normal	
breast tumor GW00-231:234	27588-91	133.52	133.52	breast tumor	7.166935051
breast normal GW98-621	23656	1334.91	2669.82	breast normal	
breast tumor GW98-620	23655	212.39	424.78	breast tumor	-6.285182918
brain normal BB99-542	25507	6816.47	13632.94	brain normal	
brain normal BB99-406	25509	1984.48	3968.96	brain normal	
brain normal BB99-904	25546	2805.82	5611.64	brain normal	
brain stage 5 ALZ BB99-874	25502	467.59	935.18	brain stage 5 ALZ	-8.274178946
brain stage 5 ALZ BB99-887	25503	3104.22	6208.44	brain stage 5 ALZ	-1.24634315
brain stage 5 ALZ BB99-862	25504	1889.81	3779.62	brain stage 5 ALZ	-2.047255191
brain stage 5 ALZ BB99-927	25542	2902.29	5804.58	brain stage 5 ALZ	-1.333058837
CT lung KC	normal	103.32	206.64	CT lung	
lung 26 KC	normal	1.13	1.13	lung 26	
lung 27 KC	normal	1.51	1.51	lung 27	
lung 24 KC	COPD	1.47	1.47	lung 24	-35.82312925
lung 28 KC	COPD	0	0.00	lung 28	-52.66
lung 23 KC	COPD	1.91	1.91	lung 23	-27.57068063
lung 25 KC	COPD	1.36	1.36	lung 25	
asthmatic lung ODO3112	29321	2.68	2.68	asthmatic lung	-19.64925373
asthmatic lung ODO3433	29323	3.25	6.50	asthmatic lung	-8.101538462
asthmatic lung ODO3397	29322	26.23	52.46	asthmatic lung	-1.003812429
asthmatic lung ODO4928	29325	7.15	14.30	asthmatic lung	-3.682517483
endo cells KC	control	15.9	15.90	endo cells	
endo VEGF KC		8.26	8.26	endo VEGF	-1.924939467
endo bFGF KC		2.01	2.01	endo bFGF	-7.910447761
heart Clontech	normal	7.9	15.80	heart	
heart ( T-1 ) ischemic	29417	67.47	134.94	heart T-1	8.540506329
heart (T-14) non-obstructive DCM	29422	106.83	213.66	heart T-14	13.52278481
heart (T-3399) DCM	29426	425.28	850.56	heart T-3399	53.83291139
adenoid GW99-269	26162	15.98	31.96	adenoid	
tonsil GW98-280	22582	17.95	35.90	tonsil	
T cells PC00314	28453	3.18	6.36	T cells	

PBMNC KC		0	0.00	PBMNC	
monocyte KC		0.81	1.62	monocyte	
B cells PC00665	28455	2.74	5.48	B cells	
dendritic cells 28441		0	0.00	dendritic cells	
neutrophils	28440	0	0.00	neutrophils	
eosinophils	28446	0	0.00	eosinophils	
BM unstim KC		0	0.00	BM unstim	
BM stim KC		0	0.00	BM stim	0
osteo dif KC		2.34	2.34	osteo dif	
osteo undif KC		0	0.00	osteo undif	-2.34
chondrocytes		145.14	362.85	chondrocytes	
OA Synovium IP12/01	29462	320.78	320.78	OA Synovium	
OA Synovium NP10/01	29461	396.85	793.70	OA Synovium	
OA Synovium NP57/00	28464	329.87	659.74	OA Synovium	
RA Synovium NP03/01	28466	103.85	207.70	RA Synovium	
RA Synovium NP71/00	28467	617.72	1235.44	RA Synovium	
RA Synovium NP45/00	28475	63.13	126.26	RA Synovium	
OA bone (biobank)	29217	3.19	3.19	OA bone (biobank)	
OA bone Sample 1	J. Emory	126.87	253.74	OA bone	
OA bone Sample 2	J. Emory	44.76	89.52	OA bone	
Cartilage (pool)	Normal	502.66	1005.32	Cartilage (pool)	
Cartilage (pool)	OA	206.76	413.52	Cartilage (pool)	-2.431127878
PBL uninfected	28441	0	0.00	PBL uninfected	
PBL HIV IIIB	28442	0	0.00	PBL HIV IIIB	0
MRC5 uninfected (100%)	29158	0	0.00	MRC5 uninfected (100%)	
MRC5 HSV strain F	29178	17.73	35.46	MRC5 HSV strain F	35.46
W12 cells	29179	0.62	1.24	W12 cells	
Keratinocytes	29180	22.63	45.26	Keratinocytes	

5 Gene Name sbg419582PROTOCADHERIN

Disease tissues	Fold Change in Disease Population Relative to
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	Normal
colon tumor	-5.52
colon tumor	1.36
colon tumor	-1.73
colon tumor	-8.84
lung tumor	1.69
lung tumor	-3.36
lung tumor	85.66
lung tumor	-7.56
breast tumor	1.48
breast tumor	16.70
breast tumor	7.17
breast tumor	-6.29
brain stage 5 ALZ	-8.27
brain stage 5 ALZ	-1.25
brain stage 5 ALZ	-2.05
brain stage 5 ALZ	-1.33
lung 24	-35.82
lung 28	-52.66
lung 23	-27.57
asthmatic lung	-19.65
asthmatic lung	-8.10
asthmatic lung	-1.00
asthmatic lung	-3.68
endo VEGF	-1.92
endo bFGF	-7.91
heart T-1	8.54
heart T-14	13.52
heart T-3399	53.83
BM stim	0.00
osteo undif	-2.34
Cartilage (pool)	-2.43
PBL HIV IIIB	0.00
MRC5 HSV strain F	35.46

**Gene Name** sbg453915TECTORINa

Very low expression overall. Expression in female reproductive tissues suggests a protein  
5 that may be secreted by these tissue types.

Sample sbg453915TECTORIN a	Mean GOI copies (sample 1)	Mean GOI copies (sample 2)	Average GOI Copies	18S rRNA (ng)	50 ng/18S rRNA (ng)	copies of mRNA detected/ 50 ng total RNA
Subcutaneous Adipocytes Zenbio	2.70	5.41	4.06	3.06	16.34	66.26
Subcutaneous Adipose Zenbio	0.00	0.00	0.00	0.96	52.36	0.00
Adrenal Gland Clontech	3.75	5.67	4.71	0.61	81.97	386.07
Whole Brain Clontech	22.57	27.88	25.23	7.24	6.91	174.21
Fetal Brain Clontech	2.42	1.80	2.11	0.48	103.95	219.33

Cerebellum Clontech	0.00	1.93	0.97	2.17	23.04	22.24
Cervix	2.90	2.10	2.50	2.42	20.66	51.65
Colon	11.19	2.68	6.94	2.71	18.45	127.95
Endometrium	4.79	19.31	12.05	0.73	68.21	821.96
Esophagus	2.06	2.93	2.50	1.37	36.50	91.06
Heart Clontech	5.42	7.31	6.37	1.32	37.88	241.10
Hypothalamus	0.00	3.70	1.85	0.32	155.28	287.27
Ileum	3.72	18.75	11.24	2.58	19.38	217.73
Jejunum	28.49	49.80	39.15	6.60	7.58	296.55
Kidney	2.12	4.37	3.25	2.12	23.58	76.53
Liver	15.74	39.80	27.77	1.50	33.33	925.67
Fetal Liver Clontech	27.96	26.14	27.05	10.40	4.81	130.05
Lung	0.00	2.37	1.19	2.57	19.46	23.05
Mammary Gland Clontech	19.68	19.22	19.45	13.00	3.85	74.81
Myometrium	3.40	1.71	2.56	2.34	21.37	54.59
Omentum	14.33	138.99	76.66	3.94	12.69	972.84
Ovary	46.55	37.80	42.18	4.34	11.52	485.89
Pancreas	4.26	2.19	3.23	0.81	61.80	199.32
Head of Pancreas	1.93	1.52	1.73	1.57	31.85	54.94
Parotid Gland	4.04	5.93	4.99	5.48	9.12	45.48
Placenta Clontech	3.69	15.48	9.59	5.26	9.51	91.11
Prostate	7.94	28.75	18.35	3.00	16.67	305.75
Rectum	11.09	3.41	7.25	1.23	40.65	294.72
Salivary Gland Clontech	0.00	1.45	0.73	7.31	6.84	4.96
Skeletal Muscle Clontech	4.76	0.00	2.38	1.26	39.68	94.44
Skin	0.00	1.39	0.70	1.21	41.32	28.72
Small Intestine Clontech	2.20	1.41	1.81	0.98	51.07	92.19
Spleen	7.15	8.12	7.64	4.92	10.16	77.59
Stomach	1.98	0.00	0.99	2.73	18.32	18.13
Testis Clontech	6.83	2.61	4.72	0.57	87.87	414.76
Thymus Clontech	0.00	0.00	0.00	9.89	5.06	0.00
Thyroid	2.38	1.88	2.13	2.77	18.05	38.45
Trachea Clontech	1.71	9.25	5.48	9.71	5.15	28.22
Urinary Bladder	3.72	8.22	5.97	5.47	9.14	54.57
Uterus	74.31	73.54	73.93	5.34	9.36	692.18

Sample sbg453915TECTORiNa	Reg number (GSK identifier)	Mean GOI copies	copies of mRNA detected/50 ng total RNA	Sample	Fold Change in Disease Population
colon normal GW98-167	21941	131.15	262.30	colon normal	
colon tumor GW98-166	21940	85.76	171.52	colon tumor	-1.529267724
colon normal GW98-178	22080	1.82	3.64	colon normal	
colon tumor GW98-177	22060	10.14	20.28	colon tumor	5.571428571
colon normal GW98-561	23514	14.25	28.50	colon normal	
colon tumor GW98-560	23513	9.89	19.78	colon tumor	-1.440849343
colon normal GW98-894	24691	32.05	64.10	colon normal	
colon tumor GW98-893	24690	53.06	106.12	colon tumor	1.655538222
lung normal GW98-3	20742	6.9	13.80	lung normal	
lung tumor GW98-2	20741	0.81	1.62	lung tumor	-8.518518519
lung normal GW97-179	20677	1.19	2.38	lung normal	
lung tumor GW97-178	20676	0	0.00	lung tumor	-2.38
lung normal GW98-165	21922	0.91	1.82	lung normal	
lung tumor GW98-164	21921	5.99	11.98	lung tumor	6.582417582
lung normal GW98-282	22584	5.93	11.86	lung normal	
lung tumor GW98-281	22583	1.54	3.08	lung tumor	-3.850649351
breast normal GW00-392	28750	6.88	6.88	breast normal	
breast tumor GW00-391	28746	4.24	8.48	breast tumor	1.23255814
breast normal GW00-413	28798	0	0.00	breast normal	
breast tumor GW00-412	28797	13.96	27.92	breast tumor	27.92
breast normal GW00-235:238	27592-95	14.42	14.42	breast normal	
breast tumor GW00-231:234	27588-91	0	0.00	breast tumor	-14.42
breast normal GW98-621	23656	5.81	11.62	breast normal	
breast tumor GW98-620	23655	0	0.00	breast tumor	-11.62
brain normal BB99-542	25507	20.59	41.18	brain normal	
brain normal BB99-406	25509	15.98	31.96	brain normal	
brain normal BB99-904	25546	2.38	4.76	brain normal	
brain stage 5 ALZ BB99-874	25502	25.45	50.90	brain stage 5 ALZ	1.960205392
brain stage 5 ALZ BB99-887	25503	35.78	71.56	brain stage 5 ALZ	2.755840822
brain stage 5 ALZ BB99-862	25504	13.83	27.66	brain stage 5 ALZ	1.06521181
brain stage 5 ALZ BB99-927	25542	21.67	43.34	brain stage 5 ALZ	1.669062901
CT lung KC	normal	6.52	13.04	CT lung	
lung 26 KC	normal	2.1	2.10	lung 26	
lung 27 KC	normal	0.84	0.84	lung 27	
lung 24 KC	COPD	1.25	1.25	lung 24	-3.432
lung 28 KC	COPD	0	0.00	lung 28	-4.29
lung 23 KC	COPD	1.16	1.16	lung 23	-3.698275862



lung 25 KC	COPD	1.18	1.18	lung 25	
asthmatic lung ODO3112	29321	4.9	4.90	asthmatic lung	1.142191142
asthmatic lung ODO3433	29323	0.83	1.66	asthmatic lung	-2.584337349
asthmatic lung ODO3397	29322	2.46	4.92	asthmatic lung	1.146853147
asthmatic lung ODO4928	29325	6	12.00	asthmatic lung	2.797202797
endo cells KC	control	2.52	2.52	endo cells	
endo VEGF KC		1.28	1.28	endo VEGF	-1.96875
endo bFGF KC		0	0.00	endo bFGF	-2.52
heart Clontech	normal	0	0.00	heart	
heart ( T-1 ) ischemic	29417	3.58	7.16	heart T-1	7.16
heart (T-14) non-obstructive DCM	29422	0	0.00	heart T-14	0
heart (T-3399)DCM	29426	0	0.00	heart T-3399	0
adenoid GW99-269	26162	2.29	4.58	adenoid	
tonsil GW98-280	22582	1.85	3.70	tonsil	
T cells PC00314	28453	4.29	8.58	T cells	
PBMNC KC		0	0.00	PBMNC	
monocyte KC		3.39	6.78	monocyte	
B cells PC00665	28455	6.04	12.08	B cells	
dendritic cells 28441		0.83	1.66	dendritic cells	
neutrophils	28440	34.69	34.69	neutrophils	
eosinophils	28446	2.86	5.72	eosinophils	
BM unstim KC		0	0.00	BM unstim	
BM stim KC		12.8	12.80	BM stim	12.8
osteo dif KC		0	0.00	osteo dif	
osteo undif KC		0	0.00	osteo undif	0
chondrocytes		4.78	11.95	chondrocytes	
OA Synovium IP12/01	29462	18.31	18.31	OA Synovium	
OA Synovium NP10/01	29461	0	0.00	OA Synovium	
OA Synovium NP57/00	28464	11.46	22.92	OA Synovium	
RA Synovium NP03/01	28466	0.87	1.74	RA Synovium	
RA Synovium NP71/00	28467	26.95	53.90	RA Synovium	
RA Synovium NP45/00	28475	18.91	37.82	RA Synovium	
OA bone (biobank)	29217	0	0.00	OA bone (biobank)	
OA bone Sample 1	J. Emory	8.66	17.32	OA bone	
OA bone Sample 2	J. Emory	7.8	15.60	OA bone	
Cartilage (pool)	Normal	16.93	33.86	Cartilage (pool)	
Cartilage (pool)	OA	6.39	12.78	Cartilage (pool)	-2.649452269

PBL uninfected	28441	0	0.00	PBL uninfected	
PBL HIV IIIB	28442	1.15	2.30	PBL HIV IIIB	2.3
MRC5 uninfected (100%)	29158	0	0.00	MRC5 uninfected (100%)	
MRC5 HSV strain F	29178	70.84	141.68	MRC5 HSV strain F	141.68
W12 cells	29179	5.59	11.18	W12 cells	
Keratinocytes	29180	0	0.00	Keratinocytes	

Gene Name sbg453915TECTORINa

Disease tissues	Fold Change in Disease Population Relative to Normal
colon tumor	-1.53
colon tumor	5.57
colon tumor	-1.44
colon tumor	1.66
lung tumor	-8.52
lung tumor	-2.38
lung tumor	6.58
lung tumor	-3.85
breast tumor	1.23
breast tumor	27.92
breast tumor	-14.42
breast tumor	-11.62
brain stage 5 ALZ	1.96
brain stage 5 ALZ	2.76
brain stage 5 ALZ	1.07
brain stage 5 ALZ	1.67
lung 24	-3.43
lung 28	-4.29
lung 23	-3.70
asthmatic lung	1.14
asthmatic lung	-2.58
asthmatic lung	1.15
asthmatic lung	2.80
endo VEGF	-1.97
endo bFGF	-2.52
heart T-1	7.16
heart T-14	0.00
heart T-3399	0.00
BM stim	12.80
osteo undif	0.00
Cartilage (pool)	-2.65
PBL HIV IIIB	2.30
MRC5 HSV strain F	141.68

5 Gene Name SBh385630.antiinflam

Some expression in adenoid, tonsils and T-cells suggesting a role in the immune system.

Expression in GI tissues suggests a role in the digestive system and potential role in diseases of the

GI system such as IBD. Overexpression in lung (1/4) and colon tumors (1/4) suggesting a role in lung and colon cancer. Increased expression in ischemic and dilated heart samples indicating a role in Cardiovascular diseases that are consistent with cardiac hypertrophy. Expression in whole brain but not localized to hypothalamus, cerebellum or cortex.

5

Sample SBh385630.antiinflam	Mean GOI copies (sample 1)	Mean GOI copies (sample 2)	Average GOI Copies	18S rRNA (ng)	50 ng/18S rRNA (ng)	copies of mRNA detected/ 50 ng total RNA
Subcutaneous Adipocytes Zenbio	0.00	6.41	3.21	3.06	16.34	52.37
Subcutaneous Adipose Zenbio	0.00	0.00	0.00	0.96	52.36	0.00
Adrenal Gland Clontech	8.40	0.00	4.20	0.61	81.97	344.26
Whole Brain Clontech	817.17	466.76	641.97	7.24	6.91	4433.46
Fetal Brain Clontech	3.80	0.00	1.90	0.48	103.95	197.51
Cerebellum Clontech	6.66	0.00	3.33	2.17	23.04	76.73
Cervix	11.99	12.30	12.15	2.42	20.66	250.93
Colon	55.51	211.32	133.42	2.71	18.45	2461.53
Endometrium	0.00	0.00	0.00	0.73	68.21	0.00
Esophagus	11.75	30.29	21.02	1.37	36.50	767.15
Heart Clontech	0.00	0.00	0.00	1.32	37.88	0.00
Hypothalamus	0.00	0.00	0.00	0.32	155.28	0.00
Ileum	40.37	42.85	41.61	2.58	19.38	806.40
Jejunum	200.19	263.82	232.01	6.60	7.58	1757.61
Kidney	18.38	34.53	26.46	2.12	23.58	623.94
Liver	11.00	17.20	14.10	1.50	33.33	470.00
Fetal Liver Clontech	150.74	123.93	137.34	10.40	4.81	660.26
Lung	82.73	77.24	79.99	2.57	19.46	1556.13
Mammary Gland Clontech	161.37	155.19	158.28	13.00	3.85	608.77
Myometrium	5.79	9.38	7.59	2.34	21.37	162.07
Omentum	36.14	46.80	41.47	3.94	12.69	526.27
Ovary	59.25	44.29	51.77	4.34	11.52	596.43
Pancreas	6.29	6.70	6.50	0.81	61.80	401.42
Head of Pancreas	0.00	26.25	13.13	1.57	31.85	417.99
Parotid Gland	8.77	52.96	30.87	5.48	9.12	281.61
Placenta Clontech	4.11	0.00	2.06	5.26	9.51	19.53
Prostate	100.91	49.99	75.45	3.00	16.67	1257.50
Rectum	180.24	305.61	242.93	1.23	40.65	9875.00
Salivary Gland Clontech	49.36	70.01	59.69	7.31	6.84	408.24
Skeletal Muscle Clontech	0.00	0.00	0.00	1.26	39.68	0.00
Skin	18.00	3.22	10.61	1.21	41.32	438.43
Small Intestine Clontech	3.90	2.55	3.23	0.98	51.07	164.71
Spleen	9.67	5.60	7.64	4.92	10.16	77.59

Stomach	32.34	83.60	57.97	2.73	18.32	1061.72
Testis Clontech	3.53	0.00	1.77	0.57	87.87	155.10
Thymus Clontech	73.66	60.02	66.84	9.89	5.06	337.92
Thyroid	15.87	12.31	14.09	2.77	18.05	254.33
Trachea Clontech	98.68	187.11	142.90	9.71	5.15	735.81
Urinary Bladder	118.92	101.91	110.42	5.47	9.14	1009.28
Uterus	9.03	24.21	16.62	5.34	9.36	155.62

<b>Sample SBh385630.antiinflam</b>	<b>Reg number (GSK identifier)</b>	<b>Mean GOI copies</b>	<b>copies of mRNA detected/50 ng total RNA</b>	<b>Sample</b>	<b>Fold Change in Disease Population</b>
colon normal GW98-167	21941	6479.77	12959.54	colon normal	
colon tumor GW98-166	21940	7824.02	15648.04	colon tumor	1.207453351
colon normal GW98-178	22080	343.81	687.62	colon normal	
colon tumor GW98-177	22060	3011.93	6023.86	colon tumor	8.760449085
colon normal GW98-561	23514	5457.38	10914.76	colon normal	
colon tumor GW98-560	23513	4017.14	8034.28	colon tumor	-1.358523726
colon normal GW98-894	24691	14903.68	29807.36	colon normal	
colon tumor GW98-893	24690	4814.19	9628.38	colon tumor	-3.095781429
lung normal GW98-3	20742	3731.84	7463.68	lung normal	
lung tumor GW98-2	20741	719.6	1439.20	lung tumor	-5.185992218
lung normal GW97-179	20677	1090.56	2181.12	lung normal	
lung tumor GW97-178	20676	6187.22	12374.44	lung tumor	5.673433832
lung normal GW98-165	21922	8416.82	16833.64	lung normal	
lung tumor GW98-164	21921	4405.14	8810.28	lung tumor	-1.910681613
lung normal GW98-282	22584	2033.26	4066.52	lung normal	
lung tumor GW98-281	22583	1785.69	3571.38	lung tumor	-1.138641086
breast normal GW00-392	28750	1583.49	1583.49	breast normal	
breast tumor GW00-391	28746	1334.89	2669.78	breast tumor	1.686010016
breast normal GW00-413	28798	1225.92	1225.92	breast normal	
breast tumor GW00-412	28797	1213.71	2427.42	breast tumor	1.980080266
breast normal GW00-235:238	27592-95	862.26	862.26	breast normal	
breast tumor GW00-231:234	27588-91	1766.08	1766.08	breast tumor	2.048198919
breast normal GW98-621	23656	1420.57	2841.14	breast normal	
breast tumor GW98-620	23655	760.05	1520.10	breast tumor	-1.869048089
brain normal BB99-542	25507	679.48	1358.96	brain normal	
brain normal BB99-406	25509	423.69	847.38	brain normal	
brain normal BB99-904	25546	401.34	802.68	brain normal	
brain stage 5 ALZ BB99-874	25502	264.51	529.02	brain stage 5 ALZ	-1.895971167
brain stage 5 ALZ BB99-887	25503	648.88	1297.76	brain stage 5 ALZ	1.293869765
brain stage 5 ALZ BB99-862	25504	234.97	469.94	brain stage 5 ALZ	-2.134329205

brain stage 5 ALZ BB99-927	25542	404.55	809.10	brain stage 5 ALZ	-1.239657232
CT lung KC	normal	6620.85	13241.70	CT lung	
lung 26 KC	normal	320.43	320.43	lung 26	
lung 27 KC	normal	164.59	164.59	lung 27	
lung 24 KC	COPD	141.57	141.57	lung 24	-25.25392032
lung 28 KC	COPD	323.8	323.80	lung 28	-11.04137585
lung 23 KC	COPD	363.35	363.35	lung 23	-9.839541764
lung 25 KC	COPD	574.07	574.07	lung 25	
asthmatic lung ODO3112	29321	6073.99	6073.99	asthmatic lung	1.698924325
asthmatic lung ODO3433	29323	4568.41	9136.82	asthmatic lung	2.555612662
asthmatic lung ODO3397	29322	17389.11	34778.22	asthmatic lung	9.727636026
asthmatic lung ODO4928	29325	4719.27	9438.54	asthmatic lung	2.640005203
endo cells KC	control	0	0.00	endo cells	
endo VEGF KC		0	0.00	endo VEGF	0
endo bFGF KC		0	0.00	endo bFGF	0
heart Clontech	normal	10.63	21.26	heart	
heart ( T-1 ) ischemic	29417	599.01	1198.02	heart T-1	56.3508937
heart (T-14) non-obstructive DCM	29422	666.41	1332.82	heart T-14	62.69143932
heart (T-3399) DCM	29426	142.85	285.70	heart T-3399	13.43838194
adenoid GW99-269	26162	1138	2276.00	adenoid	
tonsil GW98-280	22582	561.57	1123.14	tonsil	
T cells PC00314	28453	736.27	1472.54	T cells	
PBMNC KC		0	0.00	PBMNC	
monocyte KC		30.38	60.76	monocyte	
B cells PC00665	28455	204.15	408.30	B cells	
dendritic cells 28441		57.66	115.32	dendritic cells	
neutrophils	28440	13.3	13.30	neutrophils	
eosinophils	28446	5.71	11.42	eosinophils	
BM unstim KC		0	0.00	BM unstim	
BM stim KC		50.38	50.38	BM stim	50.38
osteo dif KC		8.62	8.62	osteo dif	
osteo undif KC		0	0.00	osteo undif	-8.62
chondrocytes		14.98	37.45	chondrocytes	
OA Synovium IP12/01	29462	134.63	134.63	OA Synovium	
OA Synovium NP10/01	29461	73.89	147.78	OA Synovium	
OA Synovium NP57/00	28464	106.98	213.96	OA Synovium	
RA Synovium NP03/01	28466	26.59	53.18	RA Synovium	
RA Synovium NP71/00	28467	60.88	121.76	RA Synovium	
RA Synovium NP45/00	28475	60.81	121.62	RA	

				Synovium	
OA bone (biobank)	29217	98.18	98.18	OA bone (biobank)	
OA bone Sample 1	J. Emory	78.3	156.60	OA bone	
OA bone Sample 2	J. Emory	107.7	215.40	OA bone	
Cartilage (pool)	Normal	72.21	144.42	Cartilage (pool)	
Cartilage (pool)	OA	48.61	97.22	Cartilage (pool)	-1.485496811
PBL uninfected	28441	30.22	60.44	PBL uninfected	
PBL HIV IIIB	28442	21.89	43.78	PBL HIV IIIB	-1.380539059
MRC5 uninfected (100%)	29158	10.74	21.48	MRC5 uninfected (100%)	
MRC5 HSV strain F	29178	171.23	342.46	MRC5 HSV strain F	15.94320298
W12 cells	29179	1143.85	2287.70	W12 cells	
Keratinocytes	29180	388.06	776.12	Keratinocytes	

Gene Name SBh385630.antiinflam

Disease tissues	Fold Change in Disease Population Relative to Normal
colon tumor	1.21
colon tumor	8.76
colon tumor	-1.36
colon tumor	-3.10
lung tumor	-5.19
lung tumor	5.67
lung tumor	-1.91
lung tumor	-1.14
breast tumor	1.69
breast tumor	1.98
breast tumor	2.05
breast tumor	-1.87
brain stage 5 ALZ	-1.90
brain stage 5 ALZ	1.29
brain stage 5 ALZ	-2.13
brain stage 5 ALZ	-1.24
lung 24	-25.25
lung 28	-11.04
lung 23	-9.84
asthmatic lung	1.70
asthmatic lung	2.56
asthmatic lung	9.73
asthmatic lung	2.64
endo VEGF	0.00
endo bFGF	0.00
heart T-1	56.35
heart T-14	62.69
heart T-3399	13.44
BM stim	50.38

osteo undif	-8.62
Cartilage (pool)	-1.49
PBL HIV IIIB	-1.38
MRC5 HSV strain F	15.94

**Gene Name** sbg471005nAChR

Expressed in immune cells with corroborating expression in OA and RA synovium

5 suggesting a role in this disease.

High expression in whole brain but not present in cortex, cerebellum, or hypothalamus suggesting localized brain expression.

Sample sbg471005nAChR	Mean GOI copies (sample 1)	Mean GOI copies (sample 2)	Average GOI Copies	18S rRNA (ng)	50 ng/18S rRNA (ng)	copies of mRNA detecte d/50 ng total RNA
Subcutaneous Adipocytes Zenbio	32.42	2.90	17.66	3.06	16.34	288.56
Subcutaneous Adipose Zenbio	0.00	0.00	0.00	0.96	52.36	0.00
Adrenal Gland Clontech	0.00	0.00	0.00	0.61	81.97	0.00
Whole Brain Clontech	1606.00	1058.07	1332.04	7.24	6.91	9199.14
Fetal Brain Clontech	0.00	6.34	3.17	0.48	103.95	329.52
Cerebellum Clontech	10.65	0.00	5.33	2.17	23.04	122.70
Cervix	0.00	0.00	0.00	2.42	20.66	0.00
Colon	0.00	0.00	0.00	2.71	18.45	0.00
Endometrium	0.00	0.00	0.00	0.73	68.21	0.00
Esophagus	0.00	2.52	1.26	1.37	36.50	45.99
Heart Clontech	4.05	0.00	2.03	1.32	37.88	76.70
Hypothalamus	2.24	0.00	1.12	0.32	155.28	173.91
Ileum	0.00	0.00	0.00	2.58	19.38	0.00
Jejunum	20.32	41.44	30.88	6.60	7.58	233.94
Kidney	14.56	0.00	7.28	2.12	23.58	171.70
Liver	3.55	10.72	7.14	1.50	33.33	237.83
Fetal Liver Clontech	127.95	116.81	122.38	10.40	4.81	588.37
Lung	12.79	0.00	6.40	2.57	19.46	124.42
Mammary Gland Clontech	30.53	24.12	27.33	13.00	3.85	105.10
Myometrium	0.00	7.10	3.55	2.34	21.37	75.85
Omentum	8.15	0.00	4.08	3.94	12.69	51.71
Ovary	18.27	7.02	12.65	4.34	11.52	145.68
Pancreas	0.00	0.00	0.00	0.81	61.80	0.00
Head of Pancreas	0.00	0.00	0.00	1.57	31.85	0.00
Parotid Gland	0.00	0.00	0.00	5.48	9.12	0.00
Placenta Clontech	9.17	0.00	4.59	5.26	9.51	43.58
Prostate	0.00	1.35	0.68	3.00	16.67	11.25
Rectum	0.00	0.00	0.00	1.23	40.65	0.00

Salivary Gland Clontech	0.00	11.84	5.92	7.31	6.84	40.49
Skeletal Muscle Clontech	6.09	7.36	6.73	1.26	39.68	266.87
Skin	0.00	0.00	0.00	1.21	41.32	0.00
Small Intestine Clontech	0.00	0.00	0.00	0.98	51.07	0.00
Spleen	5.20	7.36	6.28	4.92	10.16	63.82
Stomach	12.85	6.38	9.62	2.73	18.32	176.10
Testis Clontech	0.00	2.25	1.13	0.57	87.87	98.86
Thymus Clontech	177.85	168.23	173.04	9.89	5.06	874.82
Thyroid	6.44	0.00	3.22	2.77	18.05	58.12
Trachea Clontech	5.07	0.00	2.54	9.71	5.15	13.05
Urinary Bladder	0.00	0.00	0.00	5.47	9.14	0.00
Uterus	29.20	10.39	19.80	5.34	9.36	185.35

Sample sbg471005nA ChR	Reg number (GSK identifier)	Mean GOI copies	copies of mRNA detected/50 ng total RNA	Sample	Fold Change in Disease Population
colon normal GW98-167	21941	1530.09	3060.18	colon normal	
colon tumor GW98-166	21940	617.15	1234.30	colon tumor	-2.479283805
colon normal GW98-178	22080	406.03	812.06	colon normal	
colon tumor GW98-177	22060	1231.53	2463.06	colon tumor	3.033101002
colon normal GW98-561	23514	844.37	1688.74	colon normal	
colon tumor GW98-560	23513	633.99	1267.98	colon tumor	-1.331834887
colon normal GW98-894	24691	1130.51	2261.02	colon normal	
colon tumor GW98-893	24690	721.29	1442.58	colon tumor	-1.567344619
lung normal GW98-3	20742	2433.65	4867.30	lung normal	
lung tumor GW98-2	20741	334.04	668.08	lung tumor	-7.28550473
lung normal GW97-179	20677	823.51	1647.02	lung normal	
lung tumor GW97-178	20676	1492	2984.00	lung tumor	1.811756991
lung normal GW98-165	21922	829.65	1659.30	lung normal	
lung tumor GW98-164	21921	595.31	1190.62	lung tumor	-1.393643648
lung normal GW98-282	22584	357.69	715.38	lung normal	
lung tumor GW98-281	22583	256.76	513.52	lung tumor	-1.393090824
breast normal GW00-392	28750	357.44	357.44	breast normal	
breast tumor GW00-391	28746	280.98	561.96	breast tumor	1.572179946
breast normal GW00-413	28798	286.18	286.18	breast normal	
breast tumor GW00-412	28797	195.5	391.00	breast tumor	1.366272975
breast normal GW00-235:238	27592-95	161.68	161.68	breast normal	
breast tumor GW00-231:234	27588-91	217.83	217.83	breast tumor	1.347290945
breast normal GW98-621	23656	531.53	1063.06	breast normal	
breast tumor GW98-620	23655	556.17	1112.34	breast tumor	1.046356744
brain normal BB99-542	25507	143.72	287.44	brain normal	



brain normal BB99-406	25509	569.17	1138.34	brain normal	
brain normal BB99-904	25546	106.85	213.70	brain normal	
brain stage 5 ALZ BB99-874	25502	286.37	572.74	brain stage 5 ALZ	1.048027423
brain stage 5 ALZ BB99-887	25503	746.74	1493.48	brain stage 5 ALZ	2.732842121
brain stage 5 ALZ BB99-862	25504	382.97	765.94	brain stage 5 ALZ	1.401554151
brain stage 5 ALZ BB99-927	25542	367.49	734.98	brain stage 5 ALZ	1.344902042
CT lung KC	normal	175.41	350.82	CT lung	
lung 26 KC	normal	20.66	20.66	lung 26	
lung 27 KC	normal	13.06	13.06	lung 27	
lung 24 KC	COPD	15.89	15.89	lung 24	-6.182662052
lung 28 KC	COPD	7.34	7.34	lung 28	-13.38453678
lung 23 KC	COPD	22.3	22.30	lung 23	-4.405493274
lung 25 KC	COPD	8.43	8.43	lung 25	
asthmatic lung ODO3112	29321	264.47	264.47	asthmatic lung	2.692012113
asthmatic lung ODO3433	29323	442.3	884.60	asthmatic lung	9.004249688
asthmatic lung ODO3397	29322	670.04	1340.08	asthmatic lung	13.64053236
asthmatic lung ODO4928	29325	414.13	828.26	asthmatic lung	8.430770797
endo cells KC	control	66.94	66.94	endo cells	
endo VEGF KC		18.49	18.49	endo VEGF	-3.620335316
endo bFGF KC		15.93	15.93	endo bFGF	-4.202134338
heart Clontech	normal	180.76	361.52	heart	
heart ( T-1 ) ischemic	29417	161.9	323.80	heart T-1	-1.116491662
heart (T-14) non-obstructive DCM	29422	141.03	282.06	heart T-14	-1.281713111
heart (T-3399) DCM	29426	321.32	642.64	heart T-3399	1.777605665
adenoid GW99-269	26162	193.61	387.22	adenoid	
tonsil GW98-280	22582	625.4	1250.80	tonsil	
T cells PC00314	28453	140.44	280.88	T cells	
PBMNC KC		0	0.00	PBMNC	
monocyte KC		0	0.00	monocyte	
B cells PC00665	28455	476.72	953.44	B cells	
dendritic cells 28441		205.79	411.58	dendritic cells	
neutrophils	28440	1366.99	1366.99	neutrophils	
eosinophils	28446	316.57	633.14	eosinophils	
BM unstim KC		29.41	29.41	BM unstim	
BM stim KC		46.03	46.03	BM stim	1.565113907
osteo dif KC		17.47	17.47	osteo dif	
osteo undif KC		1.87	1.87	osteo undif	-9.342245989
chondrocytes		735.88	1839.70	chondrocytes	
OA Synovium IP12/01	29462	686.8	686.80	OA Synovium	
OA Synovium NP10/01	29461	4887.16	9774.32	OA	

				Synovium	
OA Synovium NP57/00	28464	721.49	1442.98	OA Synovium	
RA Synovium NP03/01	28466	383.33	766.66	RA Synovium	
RA Synovium NP71/00	28467	780.94	1561.88	RA Synovium	
RA Synovium NP45/00	28475	543.62	1087.24	RA Synovium	
OA bone (biobank)	29217	780.12	780.12	OA bone (biobank)	
OA bone Sample 1	J. Emory	361.65	723.30	OA bone	
OA bone Sample 2	J. Emory	197.57	395.14	OA bone	
Cartilage (pool)	Normal	220.7	441.40	Cartilage (pool)	
Cartilage (pool)	OA	75.52	151.04	Cartilage (pool)	-2.922404661
PBL uninfected	28441	1745.81	3491.62	PBL uninfected	
PBL HIV IIIB	28442	832.4	1664.80	PBL HIV IIIB	-2.097321
MRC5 uninfected (100%)	29158	147.92	295.84	MRC5 uninfected (100%)	
MRC5 HSV strain F	29178	146	292.00	MRC5 HSV strain F	-1.013150685
W12 cells	29179	304.27	608.54	W12 cells	
Keratinocytes	29180	139.44	278.88	Keratinocytes	

Gene Name sbg471005nAChR

Disease tissues	Fold Change in Disease Population Relative to Normal
colon tumor	-2.48
colon tumor	3.03
colon tumor	-1.33
colon tumor	-1.57
lung tumor	-7.29
lung tumor	1.81
lung tumor	-1.39
lung tumor	-1.39
breast tumor	1.57
breast tumor	1.37
breast tumor	1.35
breast tumor	1.05
brain stage 5 ALZ	1.05
brain stage 5 ALZ	2.73
brain stage 5 ALZ	1.40
brain stage 5 ALZ	1.34
lung 24	-6.18
lung 28	-13.38
lung 23	-4.41
asthmatic lung	2.69

asthmatic lung	9.00
asthmatic lung	13.64
asthmatic lung	8.43
endo VEGF	-3.62
endo bFGF	-4.20
heart T-1	-1.12
heart T-14	-1.28
heart T-3399	1.78
BM stim	1.57
osteo undif	-9.34
Cartilage (pool)	-2.92
PBL HIV IIIB	-2.10
MRC5 HSV strain F	-1.01

**Gene Name** sbg442445PROa

5 Strong expression in B-cells with expression in other immune cell types indicate function in immune system. Corroborating expression in RA and OA samples indicate role in disease. 2X increase in cells infected with HIV suggests possible marker in HIV infection. Expression in whole brain but not cortex or cerebellum suggests localized expression in brain.

Sample sbg442445PROa	Mean GOI copies (sample 1)	Mean GOI copies (sample 2)	Average GOI Copies	18S rRNA (ng)	50 ng/18S rRNA (ng)	copies of mRNA detecte d/50 ng total RNA
Subcutaneous Adipocytes Zenbio	1.13	3.82	2.48	3.06	16.34	40.44
Subcutaneous Adipose Zenbio	0.63	0	0.32	0.96	52.36	16.49
Adrenal Gland Clontech	0.64	0.74	0.69	0.61	81.97	56.56
Whole Brain Clontech	368.87	396.51	382.69	7.24	6.91	2642.89
Fetal Brain Clontech	1.57	2.5	2.04	0.48	103.95	211.54
Cerebellum Clontech	1.63	0	0.82	2.17	23.04	18.78
Cervix	4.57	5.6	5.09	2.42	20.66	105.06
Colon	18.13	7.38	12.76	2.71	18.45	235.33
Endometrium	4.23	0	2.12	0.73	68.21	144.27
Esophagus	6.85	12.66	9.76	1.37	36.50	356.02
Heart Clontech	12.83	1.44	7.14	1.32	37.88	270.27
Hypothalamus	0.58	7.26	3.92	0.32	155.28	608.70
Ileum	22.89	6.34	14.62	2.58	19.38	283.24
Jejunum	6.67	36.71	21.69	6.60	7.58	164.32
Kidney	2.82	6.28	4.55	2.12	23.58	107.31
Liver	11.21	1.24	6.23	1.50	33.33	207.50
Fetal Liver Clontech	118	135.81	126.91	10.40	4.81	610.12
Lung	13.95	37.87	25.91	2.57	19.46	504.09
Mammary Gland Clontech	15.77	11.19	13.48	13.00	3.85	51.85
Myometrium	16.26	49.21	32.74	2.34	21.37	699.47
Omentum	16.64	25.59	21.12	3.94	12.69	267.96
Ovary	4.98	7.48	6.23	4.34	11.52	71.77

Pancreas	1.23	0	0.62	0.81	61.80	38.01
Head of Pancreas	3.57	0	1.79	1.57	31.85	56.85
Parotid Gland	0.59	0	0.30	5.48	9.12	2.69
Placenta Clontech	2.67	2.75	2.71	5.26	9.51	25.76
Prostate	9.23	7.92	8.58	3.00	16.67	142.92
Rectum	2.62	4.28	3.45	1.23	40.65	140.24
Salivary Gland Clontech	1.02	14.59	7.81	7.31	6.84	53.39
Skeletal Muscle Clontech	0	0.98	0.49	1.26	39.68	19.44
Skin	2.72	0	1.36	1.21	41.32	56.20
Small Intestine Clontech	0.99	1	1.00	0.98	51.07	50.82
Spleen	31.29	42.16	36.73	4.92	10.16	373.22
Stomach	15.74		7.87	2.73	18.32	144.14
Testis Clontech	4.63	2.77	3.70	0.57	87.87	325.13
Thymus Clontech	503.91	615.6	559.76	9.89	5.06	2829.90
Thyroid	0.75	10.38	5.57	2.77	18.05	100.45
Trachea Clontech	65.95	52.98	59.47	9.71	5.15	306.20
Urinary Bladder	9.1	3.76	6.43	5.47	9.14	58.78
Uterus	13.88	4.35	9.12	5.34	9.36	85.35

Sample sbg442445PROa	Reg number (GSK identifier)	Mean GOI copies	copies of mRNA detected/50 ng total RNA	Sample	Fold Change in Disease Population
colon normal GW98-167	21941	392.89	785.78	colon normal	
colon tumor GW98-166	21940	466.75	933.50	colon tumor	1.18799155
colon normal GW98-178	22080	113.54	227.08	colon normal	
colon tumor GW98-177	22060	43.88	87.76	colon tumor	-2.587511395
colon normal GW98-561	23514	335.16	670.32	colon normal	
colon tumor GW98-560	23513	173.85	347.70	colon tumor	-1.927868852
colon normal GW98-894	24691	288.76	577.52	colon normal	
colon tumor GW98-893	24690	164.44	328.88	colon tumor	-1.756020433
lung normal GW98-3	20742	2119.16	4238.32	lung normal	
lung tumor GW98-2	20741	33.63	67.26	lung tumor	-63.01397562
lung normal GW97-179	20677	1213.42	2426.84	lung normal	
lung tumor GW97-178	20676	2011.79	4023.58	lung tumor	1.657950256
lung normal GW98-165	21922	2088.93	4177.86	lung normal	
lung tumor GW98-164	21921	862.54	1725.08	lung tumor	-2.421835509
lung normal GW98-282	22584	499.54	999.08	lung normal	
lung tumor GW98-281	22583	946.36	1892.72	lung tumor	1.894462906
breast normal GW00-392	28750	208.96	208.96	breast normal	
breast tumor GW00-391	28746	259.34	518.68	breast tumor	2.48219755
breast normal GW00-413	28798	65.02	65.02	breast normal	
breast tumor GW00-412	28797	493.02	986.04	breast tumor	15.16517994
breast normal GW00-235:238	27592-95	24.18	24.18	breast normal	

breast tumor GW00-231:234	27588-91	126.63	126.63	breast tumor	5.236972705
breast normal GW98-621	23656	536.09	1072.18	breast normal	
breast tumor GW98-620	23655	203.7	407.40	breast tumor	-2.631762396
brain normal BB99-542	25507	88.47	176.94	brain normal	
brain normal BB99-406	25509	147.87	295.74	brain normal	
brain normal BB99-904	25546	35.13	70.26	brain normal	
brain stage 5 ALZ BB99-874	25502	75.02	150.04	brain stage 5 ALZ	-1.206211677
brain stage 5 ALZ BB99-887	25503	189	378.00	brain stage 5 ALZ	2.088628578
brain stage 5 ALZ BB99-862	25504	131.38	262.76	brain stage 5 ALZ	1.451873135
brain stage 5 ALZ BB99-927	25542	36.77	73.54	brain stage 5 ALZ	-2.46097362
CT lung KC	normal	1441.16	2882.32	CT lung	
lung 26 KC	normal	69.7	69.70	lung 26	
lung 27 KC	normal	59.95	59.95	lung 27	
lung 24 KC	COPD	5.33	5.33	lung 24	-142.0727017
lung 28 KC	COPD	30.24	30.24	lung 28	-25.04125331
lung 23 KC	COPD	52.96	52.96	lung 23	-14.29847998
lung 25 KC	COPD	17.02	17.02	lung 25	
asthmatic lung ODO3112	29321	309.94	309.94	asthmatic lung	-2.44320675
asthmatic lung ODO3433	29323	532.32	1064.64	asthmatic lung	1.405933991
asthmatic lung ODO3397	29322	1159.05	2318.10	asthmatic lung	3.061218426
asthmatic lung ODO4928	29325	873.73	1747.46	asthmatic lung	2.307647103
endo cells KC	control	0	0.00	endo cells	
endo VEGF KC		0.93	0.93	endo VEGF	0.93
endo bFGF KC		5.16	5.16	endo bFGF	5.16
heart Clontech	normal	43.01	86.02	heart	
heart ( T-1 ) ischemic	29417	81.55	163.10	heart T-1	1.896070681
heart (T-14) non-obstructive DCM	29422	51.64	103.28	heart T-14	1.200651011
heart (T-3399) DCM	29426	90.27	180.54	heart T-3399	2.098814229
adenoid GW99-269	26162	982.05	1964.10	adenoid	
tonsil GW98-280	22582	3981.71	7963.42	tonsil	
T cells PC00314	28453	265.95	531.90	T cells	
PBMNC KC		40.89	40.89	PBMNC	
monocyte KC		62.92	125.84	monocyte	
B cells PC00665	28455	9045.58	18091.16	B cells	
dendritic cells 28441		267.47	534.94	dendritic cells	
neutrophils	28440	1212.1	1212.10	neutrophils	
eosinophils	28446	1563.76	3127.52	eosinophils	
BM unstim KC		56.55	56.55	BM unstim	
BM stim KC		27.4	27.40	BM stim	-2.063868613
osteo dif KC		0	0.00	osteo dif	
osteo undif KC		0	0.00	osteo undif	0

chondrocytes		0.92	2.30	chondrocytes	
OA Synovium IP12/01	29462	524.44	524.44	OA Synovium	
OA Synovium NP10/01	29461	191.8	383.60	OA Synovium	
OA Synovium NP57/00	28464	461.09	922.18	OA Synovium	
RA Synovium NP03/01	28466	484.63	969.26	RA Synovium	
RA Synovium NP71/00	28467	698.08	1396.16	RA Synovium	
RA Synovium NP45/00	28475	1034.78	2069.56	RA Synovium	
OA bone (biobank)	29217	547.68	547.68	OA bone (biobank)	
OA bone Sample 1	J. Emory	286.6	573.20	OA bone	
OA bone Sample 2	J. Emory	604.86	1209.72	OA bone	
Cartilage (pool)	Normal	224.68	449.36	Cartilage (pool)	
Cartilage (pool)	OA	113.78	227.56	Cartilage (pool)	-1.974687994
PBL uninfected	28441	966.68	1933.36	PBL uninfected	
PBL HIV IIIB	28442	1353.87	2707.74	PBL HIV IIIB	1.400535855
MRC5 uninfected (100%)	29158	1.28	2.56	MRC5 uninfected (100%)	
MRC5 HSV strain F	29178	34.07	68.14	MRC5 HSV strain F	26.6171875
W12 cells	29179	3.55	7.10	W12 cells	
Keratinocytes	29180	5.64	11.28	Keratinocytes	

Gene Name sbg442445PROa

Disease tissues	Fold Change in Disease Population Relative to Normal
colon tumor	1.19
colon tumor	-2.59
colon tumor	-1.93
colon tumor	-1.76
lung tumor	-63.01
lung tumor	1.66
lung tumor	-2.42
lung tumor	1.89
breast tumor	2.48
breast tumor	15.17
breast tumor	5.24
breast tumor	-2.63
brain stage 5 ALZ	-1.21
brain stage 5 ALZ	2.09
brain stage 5 ALZ	1.45
brain stage 5 ALZ	-2.46
lung 24	-142.07
lung 28	-25.04
lung 23	-14.30
asthmatic lung	-2.44

asthmatic lung	1.41
asthmatic lung	3.06
asthmatic lung	2.31
endo VEGF	0.93
endo bFGF	5.16
heart T-1	1.90
heart T-14	1.20
heart T-3399	2.10
BM stim	-2.06
osteo undif	0.00
Cartilage (pool)	-1.97
PBL HIV IIIB	1.40
MRC5 HSV strain F	26.62

**Gene Name** sbg456548CytoRa

Strongly expressed in adenoid/tonsils and dendritic cells. Overexpressed in stimulated bone marrow. Taken together, these data suggest a role in immune function. Expression in GI tract suggests potential role in diseases of the GI system like IBD, Chron's, etc.

5

Sample sbg456548CytoRa	Mean GOI copies (sample 1)	Mean GOI copies (sample 2)	Average GOI Copies	18S rRNA (ng)	50 ng/18S rRNA (ng)	copies of mRNA detected/ 50 ng total RNA
Subcutaneous Adipocytes Zenbio	0.00	5.06	2.53	3.06	16.34	41.34
Subcutaneous Adipose Zenbio	0.00	0.00	0.00	0.96	52.36	0.00
Adrenal Gland Clontech	0.00	0.00	0.00	0.61	81.97	0.00
Whole Brain Clontech	0.00	0.00	0.00	7.24	6.91	0.00
Fetal Brain Clontech	0.00	0.00	0.00	0.48	103.95	0.00
Cerebellum Clontech	0.00	0.00	0.00	2.17	23.04	0.00
Cervix	0.00	7.86	3.93	2.42	20.66	81.20
Colon	9.12	37.61	23.37	2.71	18.45	431.09
Endometrium	0.00	0.00	0.00	0.73	68.21	0.00
Esophagus	0.00	0.00	0.00	1.37	36.50	0.00
Heart Clontech	0.00	0.00	0.00	1.32	37.88	0.00
Hypothalamus	0.00	0.00	0.00	0.32	155.28	0.00
Ileum	not done	39.63	39.63	2.58	19.38	768.02
Jejunum	9.16	33.67	21.42	6.60	7.58	162.23
Kidney	0.00	0.00	0.00	2.12	23.58	0.00
Liver	0.00	13.75	6.88	1.50	33.33	229.17
Fetal Liver Clontech	0.00	0.00	0.00	10.40	4.81	0.00
Lung	0.00	0.00	0.00	2.57	19.46	0.00
Mammary Gland Clontech	136.73	106.34	121.54	13.00	3.85	467.44
Myometrium	27.33	17.56	22.45	2.34	21.37	479.59
Omentum	0.00	12.61	6.31	3.94	12.69	80.01
Ovary	16.46	17.90	17.18	4.34	11.52	197.93

Pancreas	0.00	0.00	0.00	0.81	61.80	0.00
Head of Pancreas	0.00	0.00	0.00	1.57	31.85	0.00
Parotid Gland	21.25	23.72	22.49	5.48	9.12	205.16
Placenta Clontech	101.11	73.40	87.26	5.26	9.51	829.42
Prostate	8.55	0.00	4.28	3.00	16.67	71.25
Rectum	0.00	0.00	0.00	1.23	40.65	0.00
Salivary Gland Clontech	0.00	0.00	0.00	7.31	6.84	0.00
Skeletal Muscle Clontech	0.00	0.00	0.00	1.26	39.68	0.00
Skin	0.00	0.00	0.00	1.21	41.32	0.00
Small Intestine Clontech	0.00	0.00	0.00	0.98	51.07	0.00
Spleen	31.60	14.66	23.13	4.92	10.16	235.06
Stomach	0.00	7.01	3.51	2.73	18.32	64.19
Testis Clontech	0.00	0.00	0.00	0.57	87.87	0.00
Thymus Clontech	51.70	103.21	77.46	9.89	5.06	391.58
Thyroid	0.00	0.00	0.00	2.77	18.05	0.00
Trachea Clontech	0.00	0.00	0.00	9.71	5.15	0.00
Urinary Bladder	0.00	7.29	3.65	5.47	9.14	33.32
Uterus	5.98	21.02	13.50	5.34	9.36	126.40

Sample sbg456548CytoRa	Reg number (GSK identifier)	Mean GOI copies	copies of mRNA detected/50 ng total RNA	Sample	Fold Change in Disease Population
colon normal GW98-167	21941	54.19	108.38	colon normal	
colon tumor GW98-166	21940	242.87	485.74	colon tumor	4.481823215
colon normal GW98-178	22080	24.61	49.22	colon normal	
colon tumor GW98-177	22060	17.37	34.74	colon tumor	-1.416810593
colon normal GW98-561	23514	120.13	240.26	colon normal	
colon tumor GW98-560	23513	43.05	86.10	colon tumor	-2.79047619
colon normal GW98-894	24691	81.35	162.70	colon normal	
colon tumor GW98-893	24690	16.94	33.88	colon tumor	-4.802243211
lung normal GW98-3	20742	12.83	25.66	lung normal	
lung tumor GW98-2	20741	94.41	188.82	lung tumor	7.358534684
lung normal GW97-179	20677	519.7	1039.40	lung normal	
lung tumor GW97-178	20676	46.83	93.66	lung tumor	-11.09758702
lung normal GW98-165	21922	7.95	15.90	lung normal	
lung tumor GW98-164	21921	237.54	475.08	lung tumor	29.87924528
lung normal GW98-282	22584	251.04	502.08	lung normal	
lung tumor GW98-281	22583	28.16	56.32	lung tumor	-8.914772727
breast normal GW00-392	28750	138.99	138.99	breast normal	
breast tumor GW00-391	28746	147.66	295.32	breast tumor	2.124757177
breast normal GW00-413	28798	30.39	30.39	breast normal	
breast tumor GW00-412	28797	37.64	75.28	breast tumor	2.477130635
breast normal GW00-	27592-95	218.09	218.09	breast	



235:238				normal	
breast tumor GW00-231:234	27588-91	14.68	14.68	breast tumor	-14.85626703
breast normal GW98-621	23656	1888.3	3776.60	breast normal	
breast tumor GW98-620	23655	877.2	1754.40	breast tumor	-2.152644779
brain normal BB99-542	25507	0	0.00	brain normal	
brain normal BB99-406	25509	0	0.00	brain normal	
brain normal BB99-904	25546	0	0.00	brain normal	
brain stage 5 ALZ BB99-874	25502	0	0.00	brain stage 5 ALZ	0
brain stage 5 ALZ BB99-887	25503	7.32	14.64	brain stage 5 ALZ	14.64
brain stage 5 ALZ BB99-862	25504	0	0.00	brain stage 5 ALZ	0
brain stage 5 ALZ BB99-927	25542	0	0.00	brain stage 5 ALZ	0
CT lung KC	normal	10.31	20.62	CT lung	
lung 26 KC	normal	49.79	49.79	lung 26	
lung 27 KC	normal	4.11	4.11	lung 27	
lung 24 KC	COPD	0.67	0.67	lung 24	-38.10074627
lung 28 KC	COPD	19.24	19.24	lung 28	-1.326793139
lung 23 KC	COPD	3.15	3.15	lung 23	-8.103968254
lung 25 KC	COPD	27.59	27.59	lung 25	
asthmatic lung ODO3112	29321	2.95	2.95	asthmatic lung	-8.653389831
asthmatic lung ODO3433	29323	9.86	19.72	asthmatic lung	-1.294497972
asthmatic lung ODO3397	29322	24.39	48.78	asthmatic lung	1.910880423
asthmatic lung ODO4928	29325	53.84	107.68	asthmatic lung	4.218196063
endo cells KC	control	0	0.00	endo cells	
endo VEGF KC		14.65	14.65	endo VEGF	14.65
endo bFGF KC		0	0.00	endo bFGF	0
heart Clontech	normal	0	0.00	heart	
heart ( T-1 ) ischemic	29417	21.18	42.36	heart T-1	42.36
heart (T-14) non-obstructive DCM	29422	27.4	54.80	heart T-14	54.8
heart (T-3399) DCM	29426	93.27	186.54	heart T-3399	186.54
adenoid GW99-269	26162	579.69	1159.38	adenoid	
tonsil GW98-280	22582	3780.08	7560.16	tonsil	
T cells PC00314	28453	5.86	11.72	T cells	
PBMNC KC		0	0.00	PBMNC	
monocyte KC		0	0.00	monocyte	
B cells PC00665	28455	19.6	39.20	B cells	
dendritic cells 28441		580.67	1161.34	dendritic cells	
neutrophils	28440	19.76	19.76	neutrophils	
eosinophils	28446	15.12	30.24	eosinophils	
BM unstim KC		0	0.00	BM unstim	
BM stim KC		296.72	296.72	BM stim	296.72

osteo dif KC		0	0.00	osteo dif	
osteo undif KC		0	0.00	osteo undif	0
chondrocytes		15.31	38.28	chondrocytes	
OA Synovium IP12/01	29462	39.57	39.57	OA Synovium	
OA Synovium NP10/01	29461	0	0.00	OA Synovium	
OA Synovium NP57/00	28464	70.08	140.16	OA Synovium	
RA Synovium NP03/01	28466	23.73	47.46	RA Synovium	
RA Synovium NP71/00	28467	24.13	48.26	RA Synovium	
RA Synovium NP45/00	28475	51.88	103.76	RA Synovium	
OA bone (biobank)	29217	0	0.00	OA bone (biobank)	
OA bone Sample 1	J. Emory	0	0.00	OA bone	
OA bone Sample 2	J. Emory	5.45	10.90	OA bone	
Cartilage (pool)	Normal	0	0.00	Cartilage (pool)	
Cartilage (pool)	OA	0	0.00	Cartilage (pool)	0
PBL uninfected	28441	76.67	153.34	PBL uninfected	
PBL HIV IIIB	28442	13.77	27.54	PBL HIV IIIB	-5.567901235
MRC5 uninfected (100%)	29158	0	0.00	MRC5 uninfected (100%)	
MRC5 HSV strain F	29178	0	0.00	MRC5 HSV strain F	0
W12 cells	29179	0	0.00	W12 cells	
Keratinocytes	29180	0	0.00	Keratinocytes	

Gene Name sbg456548CytoRa

Disease tissues	Fold Change in Disease Population Relative to Normal
colon tumor	4.48
colon tumor	-1.42
colon tumor	-2.79
colon tumor	-4.80
lung tumor	7.36
lung tumor	-11.10
lung tumor	29.88
lung tumor	-8.91
breast tumor	2.12
breast tumor	2.48

breast tumor	-14.86
breast tumor	-2.15
brain stage 5 ALZ	0.00
brain stage 5 ALZ	14.64
brain stage 5 ALZ	0.00
brain stage 5 ALZ	0.00
lung 24	-38.10
lung 28	-1.33
lung 23	-8.10
asthmatic lung	-8.65
asthmatic lung	-1.29
asthmatic lung	1.91
asthmatic lung	4.22
endo VEGF	14.65
endo bFGF	0.00
heart T-1	42.36
heart T-14	54.80
heart T-3399	186.54
BM stim	296.72
osteo undif	0.00
Cartilage (pool)	0.00
PBL HIV IIIB	-5.57
MRC5 HSV strain F	0.00

**Gene Name** sbg442358PROa

Expression in multiple immune cell types as well as stimulated bone marrow and thymus strongly suggests function in immune system. Overexpressed in breast tumors (1/4). Expression in RA and OA with corroborating expression in immune cells suggests role in these diseases. Overexpressed in heart disease suggesting role in CV diseases. Downregulated in HSV infected cells suggesting possible host cell factor.

Sample sbg442358PROa	Mean GOI copies (sample 1)	Mean GOI copies (sample 2)	Average GOI Copies	18S rRNA (ng)	50 ng/18S rRNA (ng)	copies of mRNA detecte d/50 ng total RNA
Subcutaneous Adipocytes Zenbio	1.86	1.71	1.79	3.06	16.34	29.17
Subcutaneous Adipose Zenbio	0.71	0.73	0.72	0.96	52.36	37.70
Adrenal Gland Clontech	3.45	1.89	2.67	0.61	81.97	218.85
Whole Brain Clontech	406.27	496.60	451.44	7.24	6.91	3117.65
Fetal Brain Clontech	3.82	1.68	2.75	0.48	103.95	285.86
Cerebellum Clontech	5.84	30.51	18.18	2.17	23.04	418.78
Cervix	2.50	0.48	1.49	2.42	20.66	30.79

Colon	18.45	18.77	18.61	2.71	18.45	343.36
Endometrium	4.93	0.30	2.62	0.73	68.21	178.38
Esophagus	8.97	6.99	7.98	1.37	36.50	291.24
Heart Clontech	5.26	16.53	10.90	1.32	37.88	412.69
Hypothalamus	2.10	2.41	2.26	0.32	155.28	350.16
Ileum	18.94	12.62	15.78	2.58	19.38	305.81
Jejunum	65.51	95.24	80.38	6.60	7.58	608.90
Kidney	2.60	3.81	3.21	2.12	23.58	75.59
Liver	7.19	7.05	7.12	1.50	33.33	237.33
Fetal Liver Clontech	1252.22	1363.06	1307.64	10.40	4.81	6286.73
Lung	27.57	6.97	17.27	2.57	19.46	335.99
Mammary Gland Clontech	79.83	72.99	76.41	13.00	3.85	293.88
Myometrium	2.46	10.62	6.54	2.34	21.37	139.74
Omentum	10.40	3.27	6.84	3.94	12.69	86.74
Ovary	17.71	31.15	24.43	4.34	11.52	281.45
Pancreas	3.33	1.74	2.54	0.81	61.80	156.67
Head of Pancreas	3.82	6.17	5.00	1.57	31.85	159.08
Parotid Gland	22.77	22.54	22.66	5.48	9.12	206.71
Placenta Clontech	14.71	53.83	34.27	5.26	9.51	325.76
Prostate	16.71	19.39	18.05	3.00	16.67	300.83
Rectum	6.71	3.49	5.10	1.23	40.65	207.32
Salivary Gland Clontech	55.38	9.30	32.34	7.31	6.84	221.20
Skeletal Muscle Clontech	3.79	4.16	3.98	1.26	39.68	157.74
Skin	4.51	14.47	9.49	1.21	41.32	392.15
Small Intestine Clontech	8.12	7.87	8.00	0.98	51.07	408.32
Spleen	14.88	17.12	16.00	4.92	10.16	162.60
Stomach	21.85	11.68	16.77	2.73	18.32	307.05
Testis Clontech	22.77	11.54	17.16	0.57	87.87	1507.47
Thymus Clontech	1990.82	1374.71	1682.77	9.89	5.06	8507.41
Thyroid	16.85	2.86	9.86	2.77	18.05	177.89
Trachea Clontech	29.69	82.85	56.27	9.71	5.15	289.75
Urinary Bladder	2.32	13.42	7.87	5.47	9.14	71.94
Uterus	8.86	11.18	10.02	5.34	9.36	93.82

Sample sbg442358PROa	Reg number (GSK identifier)	Mean GOI copies	copies of mRNA detected/50 ng total RNA	Sample	Fold Change in Disease Population
colon normal GW98-167	21941	1232.32	2464.64	colon normal	
colon tumor GW98-166	21940	2940.17	5880.34	colon tumor	2.385881914
colon normal GW98-178	22080	221.26	442.52	colon normal	
colon tumor GW98-177	22060	709.52	1419.04	colon tumor	3.20672512
colon normal GW98-561	23514	985.52	1971.04	colon normal	
colon tumor GW98-560	23513	829.67	1659.34	colon tumor	-1.18784577

colon normal GW98-894	24691	2738.17	5476.34	colon normal	
colon tumor GW98-893	24690	3022.06	6044.12	colon tumor	1.103678734
lung normal GW98-3	20742	536.82	1073.64	lung normal	
lung tumor GW98-2	20741	594.2	1188.40	lung tumor	1.106888715
lung normal GW97-179	20677	4382.61	8765.22	lung normal	
lung tumor GW97-178	20676	359.07	718.14	lung tumor	-12.20544741
lung normal GW98-165	21922	622.06	1244.12	lung normal	
lung tumor GW98-164	21921	1299.85	2599.70	lung tumor	2.089589429
lung normal GW98-282	22584	1782.09	3564.18	lung normal	
lung tumor GW98-281	22583	470.51	941.02	lung tumor	-3.787570934
breast normal GW00-392	28750	429	429.00	breast normal	
breast tumor GW00-391	28746	417.99	835.98	breast tumor	1.948671329
breast normal GW00-413	28798	16.03	16.03	breast normal	
breast tumor GW00-412	28797	1048.11	2096.22	breast tumor	130.768559
breast normal GW00-235:238	27592-95	2.17	2.17	breast normal	
breast tumor GW00-231:234	27588-91	69.91	69.91	breast tumor	32.21658986
breast normal GW98-621	23656	1037.08	2074.16	breast normal	
breast tumor GW98-620	23655	1010.59	2021.18	breast tumor	-1.026212411
brain normal BB99-542	25507	299.28	598.56	brain normal	
brain normal BB99-406	25509	250.85	501.70	brain normal	
brain normal BB99-904	25546	97.7	195.40	brain normal	
brain stage 5 ALZ BB99-874	25502	125	250.00	brain stage 5 ALZ	-1.727546667
brain stage 5 ALZ BB99-887	25503	850.01	1700.02	brain stage 5 ALZ	3.936264143
brain stage 5 ALZ BB99-862	25504	347.91	695.82	brain stage 5 ALZ	1.611117114
brain stage 5 ALZ BB99-927	25542	147.11	294.22	brain stage 5 ALZ	-1.467903836
CT lung KC	normal	130.37	260.74	CT lung	
lung 26 KC	normal	159.19	159.19	lung 26	
lung 27 KC	normal	0.49	0.49	lung 27	
lung 24 KC	COPD	2.37	2.37	lung 24	-47.89873418
lung 28 KC	COPD	45.72	45.72	lung 28	-2.482939633
lung 23 KC	COPD	20.36	20.36	lung 23	-5.575638507
lung 25 KC	COPD	33.66	33.66	lung 25	
asthmatic lung ODO3112	29321	65.46	65.46	asthmatic lung	-1.734188818
asthmatic lung ODO3433	29323	532.42	1064.84	asthmatic lung	9.380197322
asthmatic lung ODO3397	29322	2865.67	5731.34	asthmatic lung	50.48749119
asthmatic lung ODO4928	29325	494.27	988.54	asthmatic lung	8.708069063
endo cells KC	control	62.77	62.77	endo cells	
endo VEGF KC		22.41	22.41	endo VEGF	-2.800981705
endo bFGF KC		33.16	33.16	endo bFGF	-1.892943305
heart Clontech	normal	74.18	148.36	heart	
heart ( T-1 ) ischemic	29417	270.07	540.14	heart T-1	3.640738744

heart (T-14) non-obstructive DCM	29422	680.12	1360.24	heart T-14	9.168509032
heart (T-3399) DCM	29426	414	828.00	heart T-3399	5.581019143
adenoid GW99-269	26162	781.46	1562.92	adenoid	
tonsil GW98-280	22582	2279.13	4558.26	tonsil	
T cells PC00314	28453	1129.27	2258.54	T cells	
PBMNC KC		27.98	27.98	PBMNC	
monocyte KC		3.55	7.10	monocyte	
B cells PC00665	28455	872.58	1745.16	B cells	
dendritic cells 28441		1055.22	2110.44	dendritic cells	
neutrophils	28440	740.39	740.39	neutrophils	
eosinophils	28446	1081.83	2163.66	eosinophils	
BM unstim KC		50.91	50.91	BM unstim	
BM stim KC		391.11	391.11	BM stim	7.682380672
osteo dif KC		161.31	161.31	osteo dif	
osteo undif KC		40.01	40.01	osteo undif	-4.031742064
chondrocytes		2250.59	5626.48	chondrocytes	
OA Synovium IP12/01	29462	229.19	229.19	OA Synovium	
OA Synovium NP10/01	29461	152.3	304.60	OA Synovium	
OA Synovium NP57/00	28464	413.06	826.12	OA Synovium	
RA Synovium NP03/01	28466	611.02	1222.04	RA Synovium	
RA Synovium NP71/00	28467	385.94	771.88	RA Synovium	
RA Synovium NP45/00	28475	1701.68	3403.36	RA Synovium	
OA bone (biobank)	29217	225.69	225.69	OA bone (biobank)	
OA bone Sample 1	J. Emory	306.63	613.26	OA bone	
OA bone Sample 2	J. Emory	1811.32	3622.64	OA bone	
Cartilage (pool)	Normal	384.44	768.88	Cartilage (pool)	
Cartilage (pool)	OA	174.53	349.06	Cartilage (pool)	-2.202715865
PBL uninfected	28441	9016.82	18033.64	PBL uninfected	
PBL HIV IIIB	28442	4331.76	8663.52	PBL HIV IIIB	-2.081560382
MRC5 uninfected (100%)	29158	2232.48	4464.96	MRC5 uninfected (100%)	
MRC5 HSV strain F	29178	419.67	839.34	MRC5 HSV strain F	-5.319608264
W12 cells	29179	3336.07	6672.14	W12 cells	
Keratinocytes	29180	5568.91	11137.82	Keratinocytes	

Gene Name sbg442358PROa

Disease tissues	Fold Change in Disease Population Relative to Normal
colon tumor	2.39

colon tumor	3.21
colon tumor	-1.19
colon tumor	1.10
lung tumor	1.11
lung tumor	-12.21
lung tumor	2.09
lung tumor	-3.79
breast tumor	1.95
breast tumor	130.77
breast tumor	32.22
breast tumor	-1.03
brain stage 5 ALZ	-1.73
brain stage 5 ALZ	3.94
brain stage 5 ALZ	1.61
brain stage 5 ALZ	-1.47
lung 24	-47.90
lung 28	-2.48
lung 23	-5.58
asthmatic lung	-1.73
asthmatic lung	9.38
asthmatic lung	50.49
asthmatic lung	8.71
endo VEGF	-2.80
endo bFGF	-1.89
heart T-1	3.64
heart T-14	9.17
heart T-3399	5.58
BM stim	7.68
osteo undif	-4.03
Cartilage (pool)	-2.20
PBL HIV IIIB	-2.08
MRC5 HSV strain F	-5.32

**Table V. Additional diseases based on mRNA expression in specific tissues**

<b>Tissue Expression</b>	<b>Additional Diseases</b>
Brain	Neurological and psychiatric diseases, including Alzheimers, parasupranuclear palsey, Huntington's disease, myotonic dystrophy, anorexia, depression, schizophrenia, headache, amnesias, anxiety disorders, sleep disorders, multiple sclerosis
Heart	Cardiovascular diseases, including congestive heart failure, dilated cardiomyopathy, cardiac arrhythmias, Hodgson's Disease, myocardial infarction, cardiac arrhythmias
Lung	Respiratory diseases, including asthma, Chronic Obstructive Pulmonary Disease, cystic fibrosis, acute bronchitis, adult respiratory distress syndrome
Liver	Dyslipidemia, hypercholesterolemia, hypertriglyceridemia, cirrhosis, hepatic encephalopathy, fatty hepatocirrhosis, viral and nonviral hepatitis, Type II Diabetes Mellitis, impaired glucose tolerance
Kidney	Renal diseases, including acute and chronic renal failure, acute tubular necrosis, cystinuria, Fanconi's Syndrome, glomerulonephritis, renal cell carcinoma, renovascular hypertension
Skeletal muscle	Eulenburg's Disease, hypoglycemia, obesity, tendinitis, periodic paralyses, malignant hyperthermia, paramyotonia congenita, myotonia congenita
Intestine	Gastrointestinal diseases, including Myotonia congenita, Ileus, Intestinal Obstruction, Tropical Sprue, Pseudomembranous Enterocolitis
Spleen/lymph	Lymphangiectasia, hypersplenism, angiomas, ankylosing spondylitis, Hodgkin's Disease, macroglobulinemia, malignant lymphomas, rheumatoid arthritis
Placenta	Choriocarcinoma, hydatidiform mole, placenta previa
Testis	Testicular cancer, male reproductive diseases, including low testosterone and male infertility
Pancreas	Diabetic ketoacidosis, Type 1 & 2 diabetes, obesity, impaired glucose tolerance

**Example - Enhanced Would Repair Mediated by sbg453915TECTORINa Homolog**

- 5 Polypeptides involved in basement membrane matrix formation and survival, proliferation and/or differentiation of cells involved in cellular regeneration and wound or joint repair are of interest. Previously, connective tissue factors such as collagen, fibronectin, laminin polypeptides and others are known to be involved in wound repair. In addition, growth and differentiation factors such as VEGF, PDGF and members of the bone morphogenic protein family have been shown to
- 10 be important in the overall tissue regeneration process. Therefore, novel polypeptides, which are related to or have the function of connective tissue proteins or growth factors or protein, which may have combined functionality of a connective tissue factor and a growth factor, are of interest.  $\beta$ -Tectorin is a naturally occurring compound that is produced in the inner ear during development and embryo growth. The function of  $\beta$ -Tectorin is not well understood but it is proposed to aid in
- 15 the transmittal of sound from the eardrum through pressure sensitive ion channels (Legan et al. (1997) J. Biol. Chem. 272(13):8791-8801).



$\beta$ -Tectorin is thus useful for treating conditions in which enhanced wound repair is required, for example, diabetic ulcers and vascular injuries resulting from trauma such as subcutaneous wounds. Being a non-collagenous connective tissue factor  $\beta$ -Tectorin enhances connective tissue matrixes allowing other cells and factors to nucleate on the  $\beta$ -Tectorin and thus lead to a stronger and faster deposition of other matrix proteins within the wound.  $\beta$ -Tectorin may also aid in the growth or formation of new or stronger blood vessels a process known as vascular neogenesis or angiogenesis. In addition,  $\beta$ -Tectorin may aid in the repair of damaged blood vessels within the wound or joint a process known as vasculogenesis.  $\beta$ -Tectorin would also find use in the regrowth and restoration of cartilage tissue in osteo or rheumatoid arthritic joints as well as other uses that can be deduced by a person knowledgeable in the art. The polypeptide encoded by sbg453915TECTORINa (SEQ ID NO:35) is the human homolog of mouse  $\beta$ -Tectorin (SEQ ID NO:46). The human and murine polypeptide homologs are 94.2% identical.

The ability of  $\beta$ -Tectorin to mediate wound repair was demonstrated in a murine model system using an adenoviral expression system to express the polypeptide *in vivo*. The open reading frame (ORF) of the gene encoding the murine  $\beta$ -Tectorin (SEQ ID NO:45; referred to herein as MPA190) was subcloned into the adenovirus shuttle vector pShuttle (ClonTech) using appropriate restriction sites, placing the ORF downstream of the CMV IE promoter in the correct orientation. An I-CeuI/PI-SceI fragment containing the expression cassette (CMV IE-ORF-BGH polyA) was isolated from the shuttle vector and was swapped with a GFP expression cassette driven by bacterial Lac promoter at the I-CeuI/PI-SceI sites of the adenovirus backbone plasmid pAdX derived from pAdeno-X (ClonTech). The cloning step was carried by a convenient green/white selection process, in which white colonies contained the recombinant construct, pAdX.MPA190. The purified molecular clone DNA of adenovirus vector was linearized by digesting with restriction enzyme PacI to expose ITRs, and transfected into HEK293 cells for adenovirus rescue. The adenovirus was amplified and purified by CsCl banding as described in Engelhardt, J. Methods in Molecular Medicine, Gene Therapy Protocols, 169-184 (P. Robbins ed., Humana Press 1999). Concentrated adenovirus was desalted by using a sterilized Bio-gel column (Bio-Rad) and stored in 1xPBS with 10% glycerol at -80oC.

Ob/ob mice are a naturally occurring strain of mice that have a natural deletion of the ob/ob gene, which codes for the cytokine protein Leptin. The resulting deletion of the ob/ob gene has numerous physiological consequences in the ob/ob mouse. These include a desire to consume food in an unrestricted manner with the result that these mice are approximately 100% heavier than the wild type mouse strain C57Bl/6. Leptin binds to a cytokine class I receptor, obRb and activates intracellular signalling cascade which curtails feeding. In addition to these mice being obese, they

also have a number of other metabolic defects including hyperphagia, reduced thermogenesis, decreased fertility, and inhibition of growth hormone production.

Leptin-deficient ob/ob mice have been used as a model system to analyze molecular characteristics of impaired wound healing. The severe wound-healing difficulties observed in ob/ob mice have been explained by the diabetic phenotype of the animals. However, growth factors and cytokines are also central to a normal wound-healing process and thus this strain of mice make a good model system for studying the human diabetic condition particularly as related to the wound repair process.

To determine the effect of  $\beta$ -Tectorin on wound repair, ob/ob mice were anesthetized and a 6 mm punch biopsy tool used to make two uniform punch biopsies on the back of the animal. Adenovirus ( $1 \times 10^{10}$  viral particles/wound or  $2 \times 10^{10}$  viral particles/mouse) coding for  $\beta$ -Tectorin or a control empty adenovirus were separately mixed with pluronic F127 gel 13% in PBS (Sigma Chemical Company Cat # P-2443) at 4°C and directly applied to the wounded area. The wound was subsequently dressed with a transparent dressing. The mice were monitored on a two-day cycle and the wound area measured as it healed. Wound area measurements were conducted by tracing the outline/margin of the healing wound through transparency film every two days. At the end of the experiment when all animals had healed, either spontaneously or with the aid of  $\beta$ -Tectorin, the transparency with the outline of the wound areas were optically scanned using a commercial scanner (Hewlett-Packard model number 7400C) and the surface area determined using Scion Image software (Scion Corporation, Frederick, Maryland, USA).

Treatment of ob/ob mice with adenovirus coding for  $\beta$ -Tectorin substantially and statistically enhanced the rate and the day of wound closure above no treatment or treatment with an empty vector adenovirus as shown in Figure 1.